Neurology For MRCPCH

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Neural Tube Defects

- **Spina bifida occulta:** failure of closure of vertebral arch**.** *5%* of population
- **Anencephaly:** Failure of closure of the rostra1 aspect of the neural tube; *75%* of affected infants are stillborn.
- **Encephalocele:** Protrusion of cerebral tissue through midline cranial defect located in frontal or occipital regions.

Encephalocele

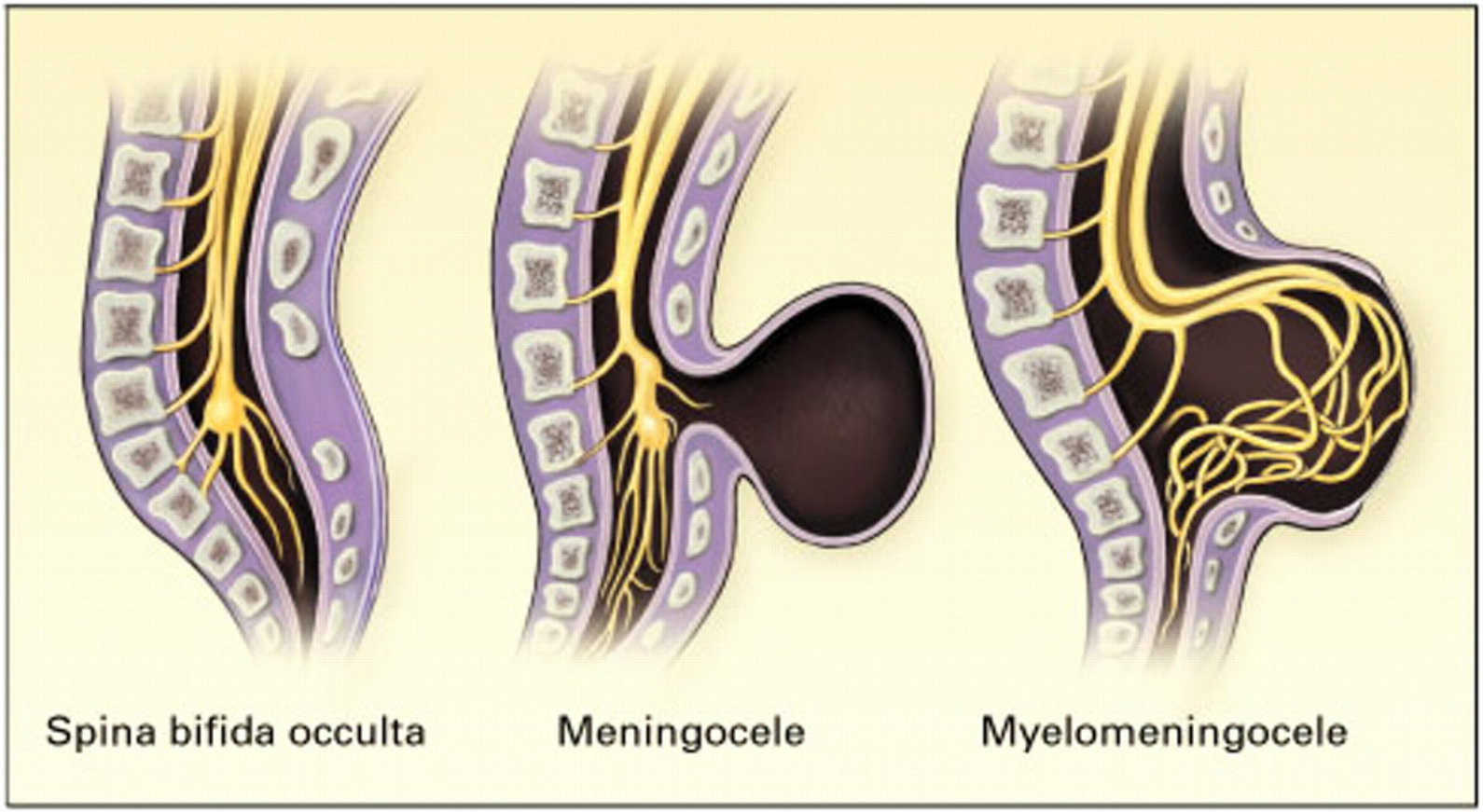


Encephalocele



Anencephaly




Spina bifida occulta
Meningocele
Myelomeningocele

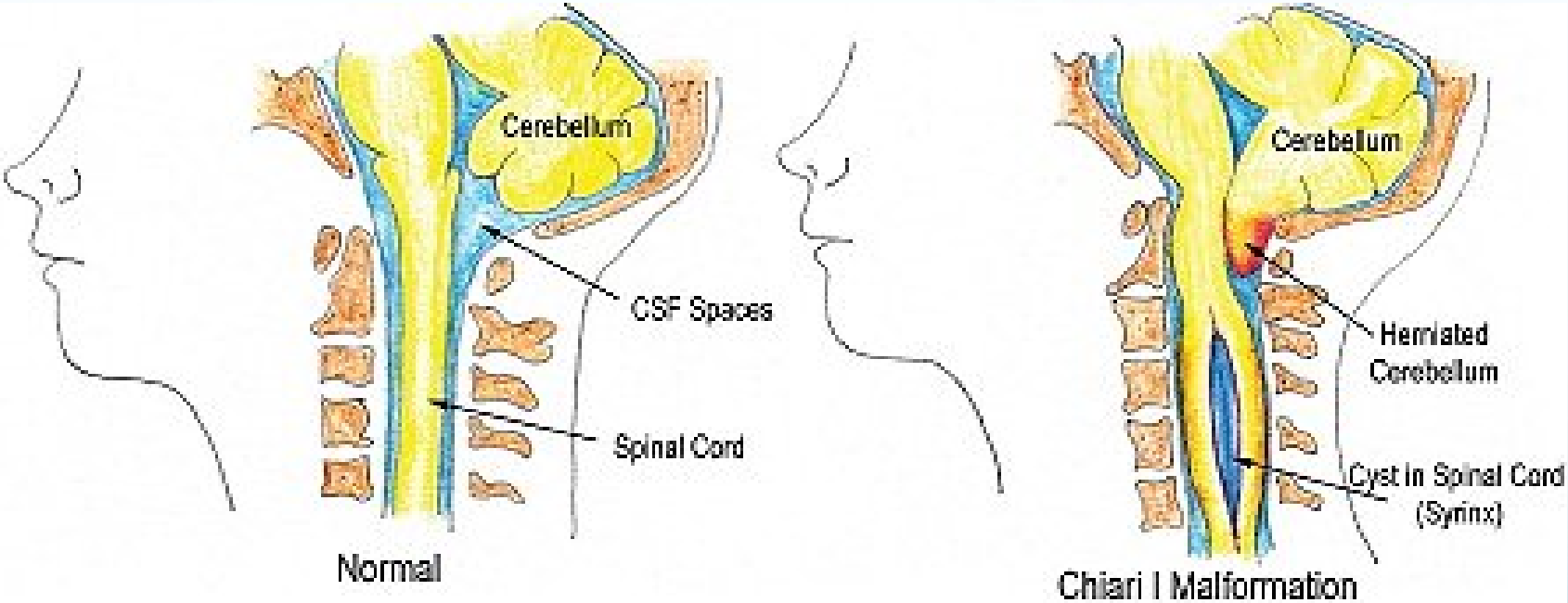
Spina bifida occulta



Neural Tube Defects

- **Meningocele:** Cyst formed by herniation of meninges, usually over dorsum of spine. Neurological disability minimal, risk of bacterial meningitis.
- **Meningomyelocele:** Herniation of meninges, nerve roots and spinal cord through dorsal vertebral defect. Leads to motor and sensory deficits below lesion, including sphincter disturbance. May be associated with other malformations of spinal cord including Arnold-Chiari malformation (downward displacement of cerebellar tonsils through foramen magnum). Hydrocephalus may coexist, secondary to Arnold-Chiari malformation or aqueduct stenosis.

Arnold Chiari Malformation



Neural Tube Defects

- **Prevention of neural tube defects:** There is clear evidence that preconceptual folate supplementation prevents production of neural tube defects.

Neural Tube Defects

- **Treatment of neural tube defects:**
- Operative repair of Encephalocele, Meningocele, myelomeningocele
- Close observation for development of hydrocephalus and operative treatment
- Management of bladder and bowels. Possible intermittent bladder drainage
- Orthopaedic management of limb deformities
- Assessment of cognitive abilities Treatment of seizures

Hydrocephalus

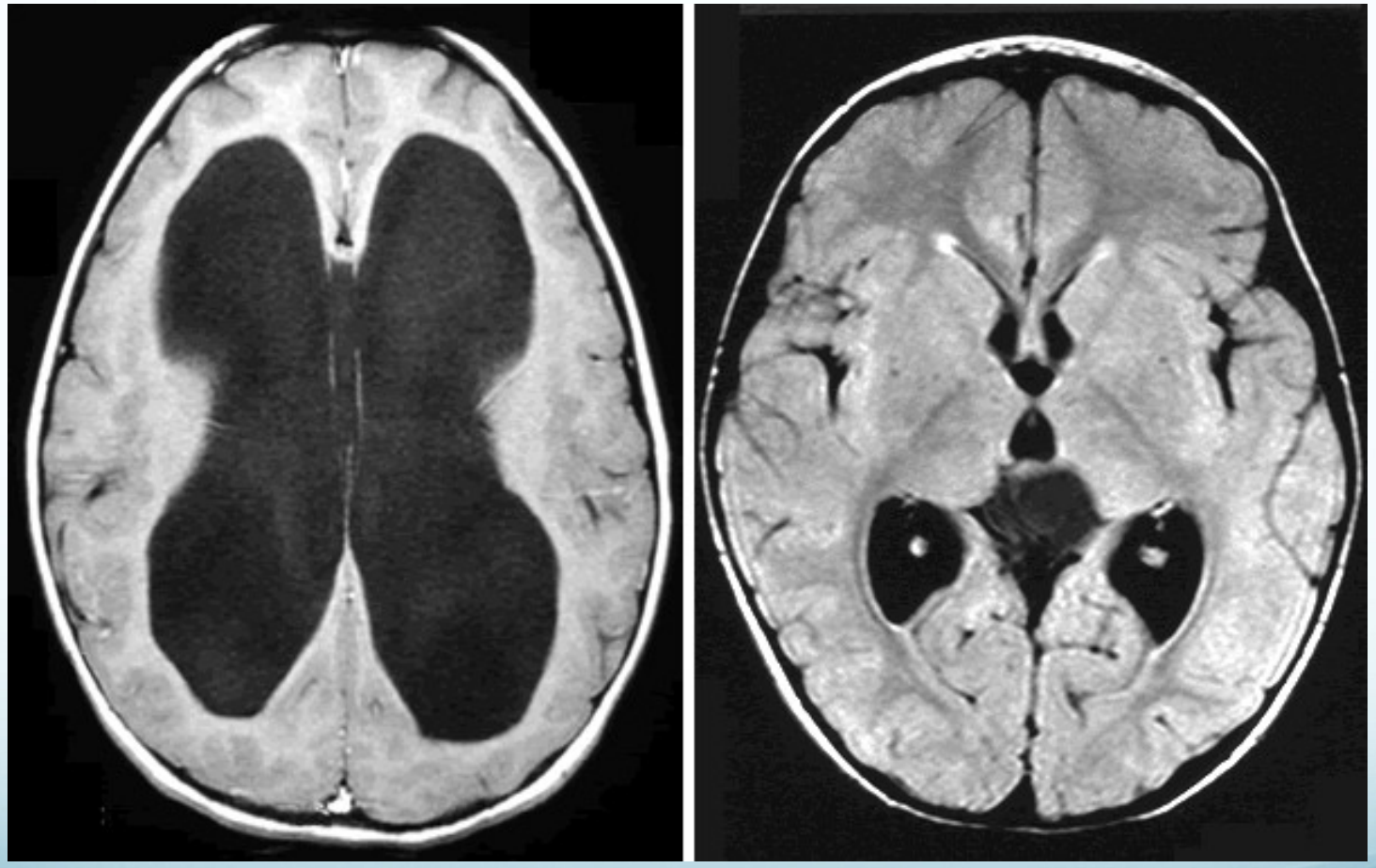
- Defined as excess fluid within the cranium. Usually refers to increased volume of cerebrospinal fluid (CSF)
- Causes:

- Over secretion
- Obstruction
- Impaired resorption

Hydrocephalus



Hydrocephalus



Clinical Diagnosis

- May be asymptomatic
- Irritability, headache and vomiting
- Drowsiness
- Increased head circumference andtense anterior fontanelle
- Splayed sutures and scalp vein distension
- Loss of upward gaze (sunsetting)
- Neck rigidity
- Decreased conscious level
- Cranial nerve palsies

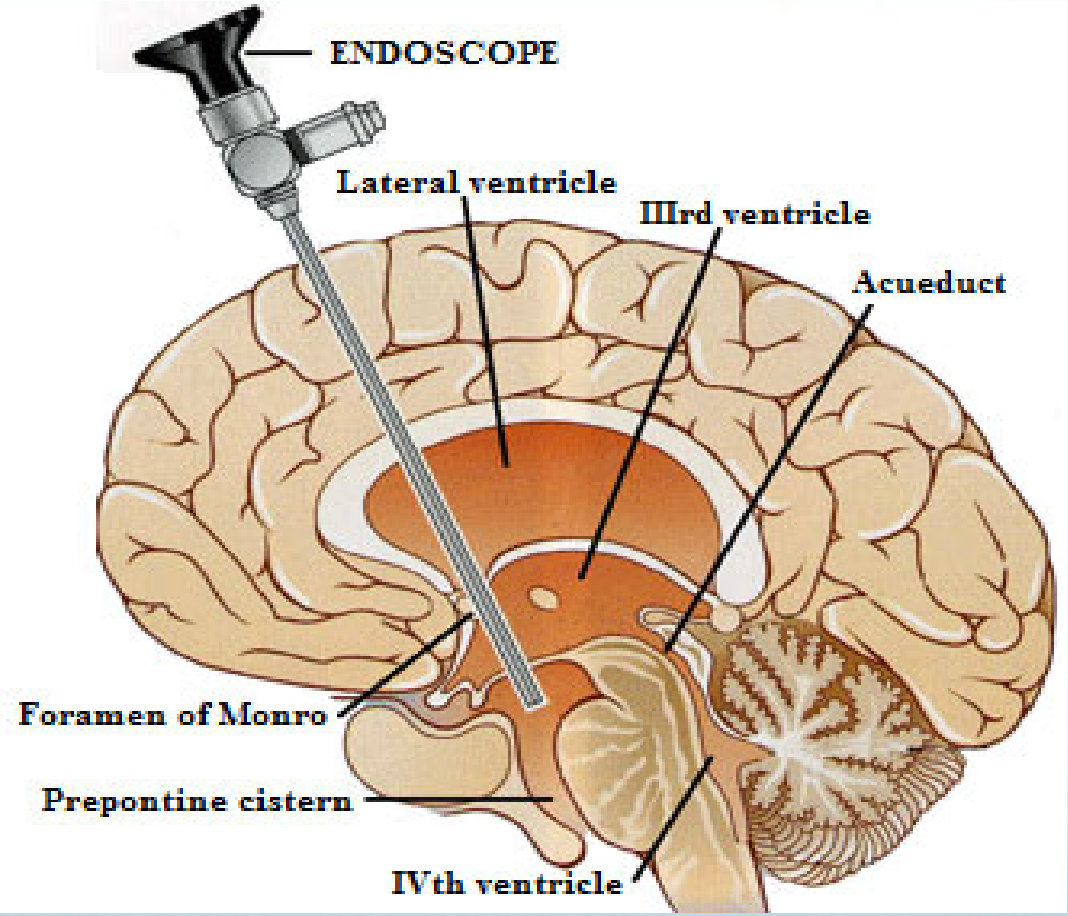
Investigations

- Ultrasonography (when fontanelle open
- Computerized tomography (CT)
- Magnetic resonance imaging (MRI)
- Measurement of CSF pressure by neurosurgical intervention may be indicated

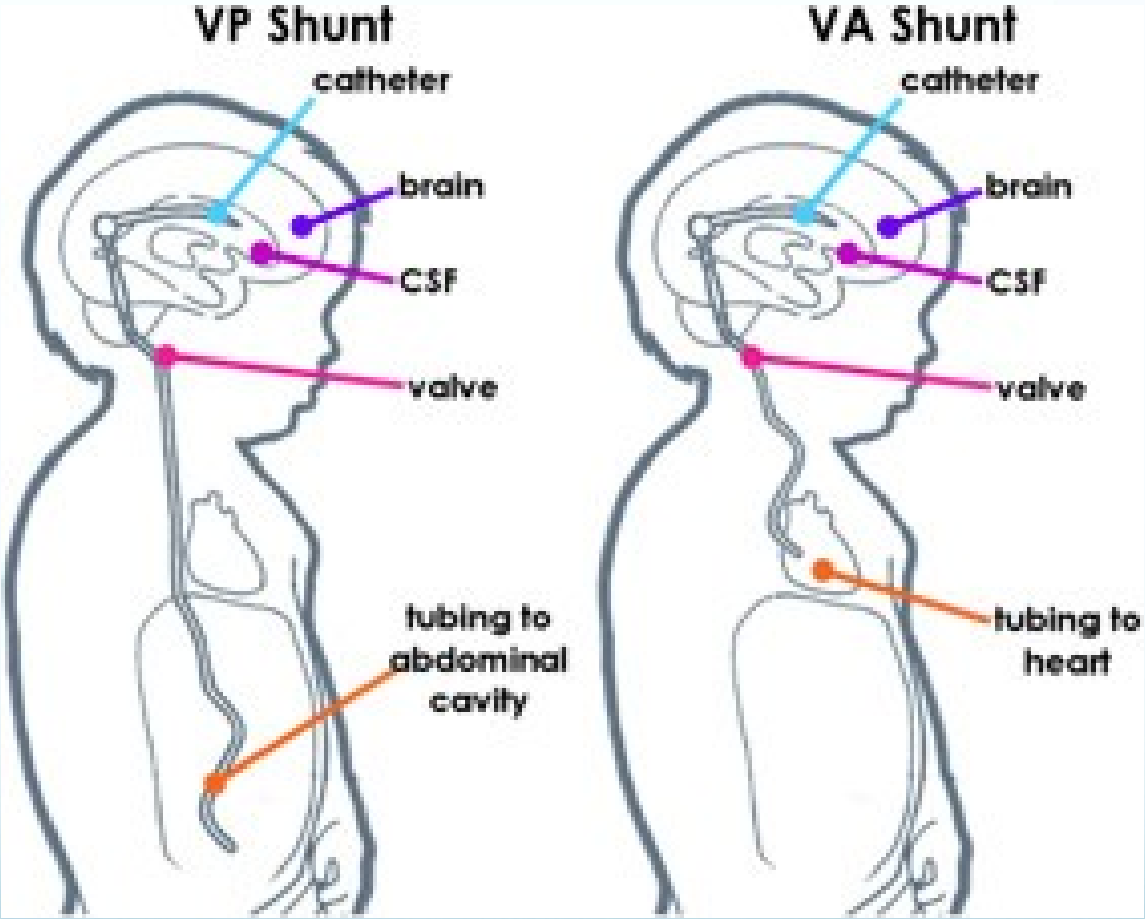
Management

- Ventriculostomy
- Shunting (ventriculoperitoneal, ventriculoatrial)

Ventriculostomy



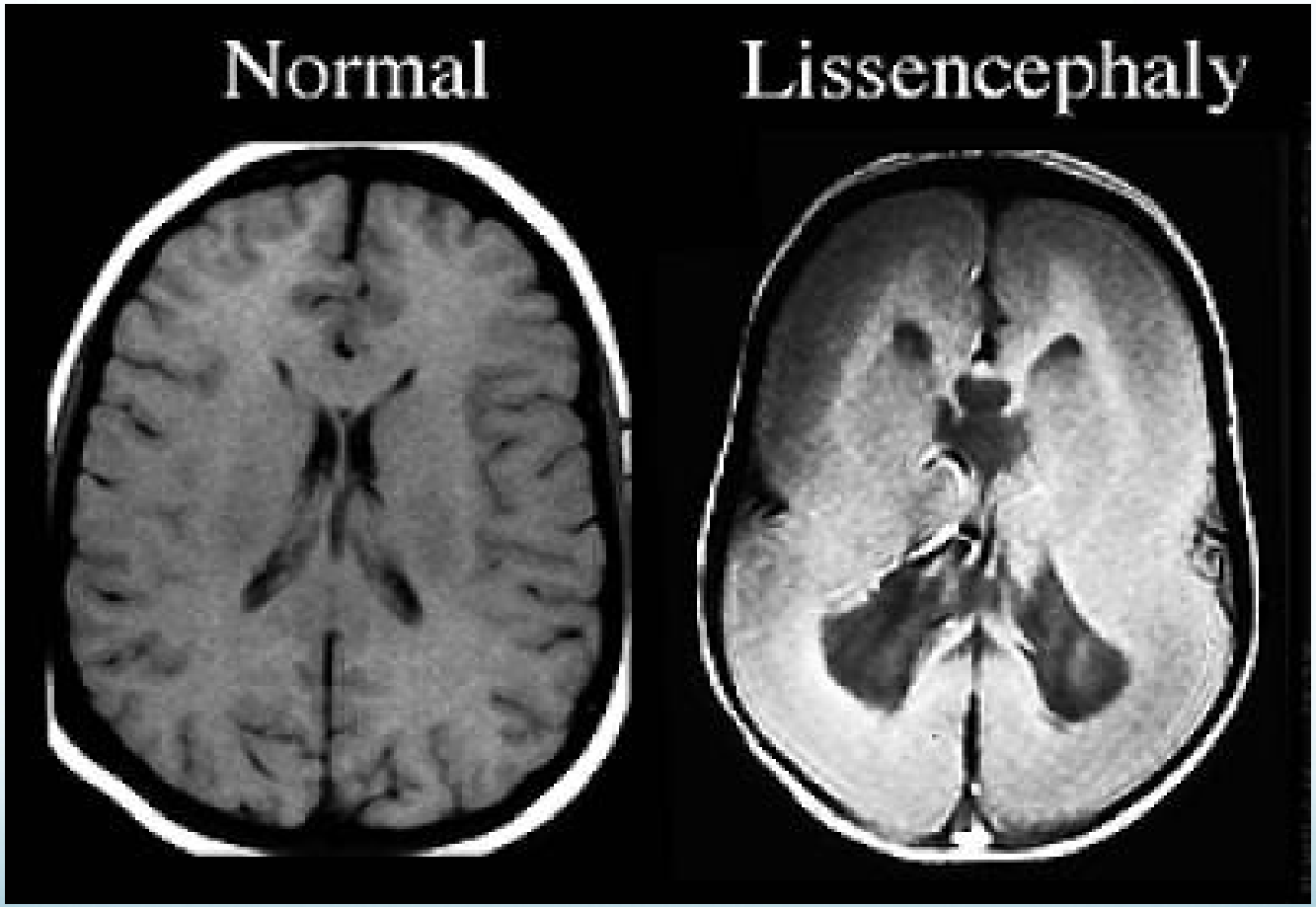
Shunt


VP Shunt
catheter
brain
CSF
valve
tubing to abdominal cavity
VA Shunt
catheter
brain
CSF
valve
tubing to heart

Disorders of Cortical Development

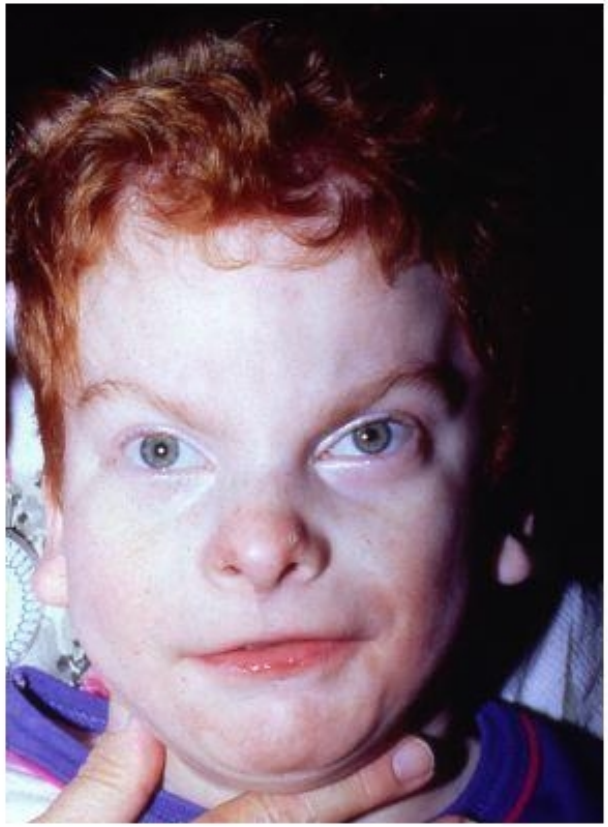
- **Lissencephaly:** Brain has very few or no gyri, leaving the surface of the brain smooth. Leads to severe motor and learning disability. Lissencephaly may be associated with facial abnormalities and a deletion on chromosome 17p13.3 in the Miller-Dieker syndrome. X-linked lissencephaly and subcortical band heterotopia ('double cortex') linked to mutations in either the doublecortin *(DCX)*or *LIS1* genes.

Lissencephaly



Miller Dieker Syndrome

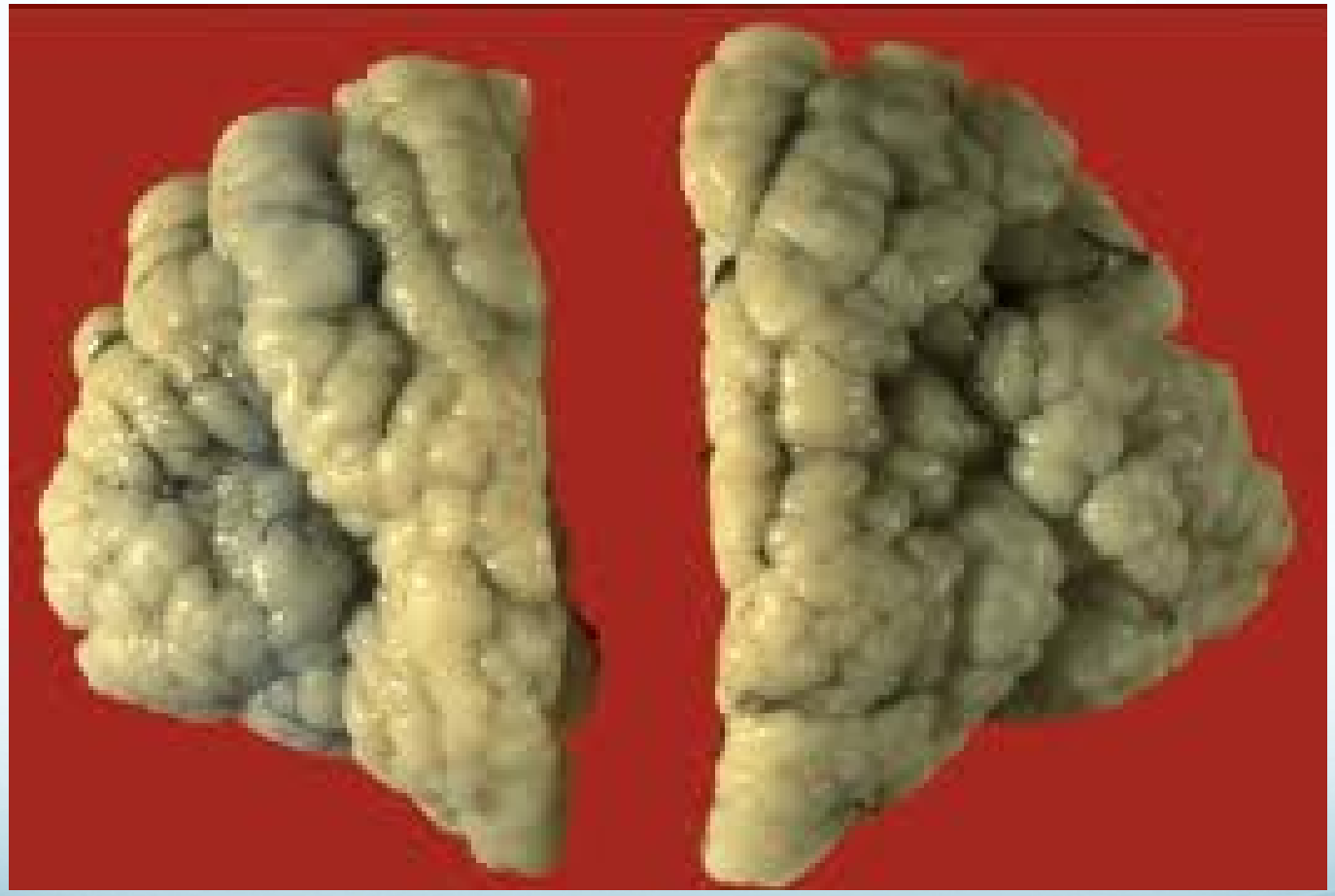




Polymicrogyria

- Focal or generalized
- Static encephalopathy

Polymicrogyria



Periventricular heterotopia

- Aggregation of neurones arrested in their primitive positions. May be part of complex brain malformation syndromes. X-linked periventricular nodular heterotopia is seen in females, characterized often by focal epilepsy and is associated in a proportion of cases with mutations in the *FLNI* gene.
- X- linked dominant
- A neural migration disorder

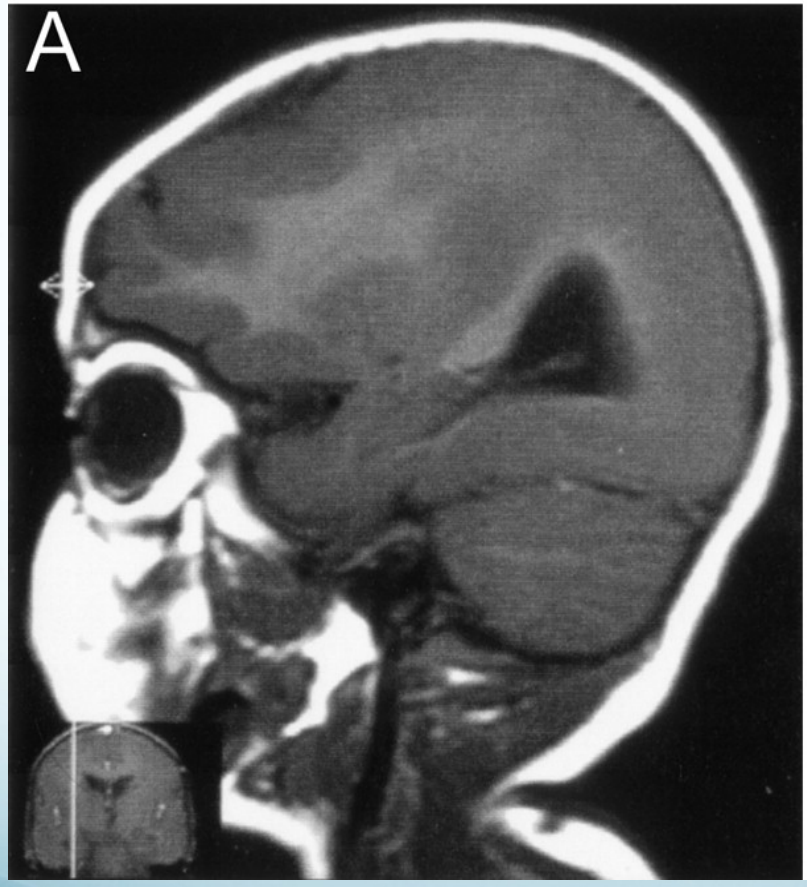
Periventricular heterotopia

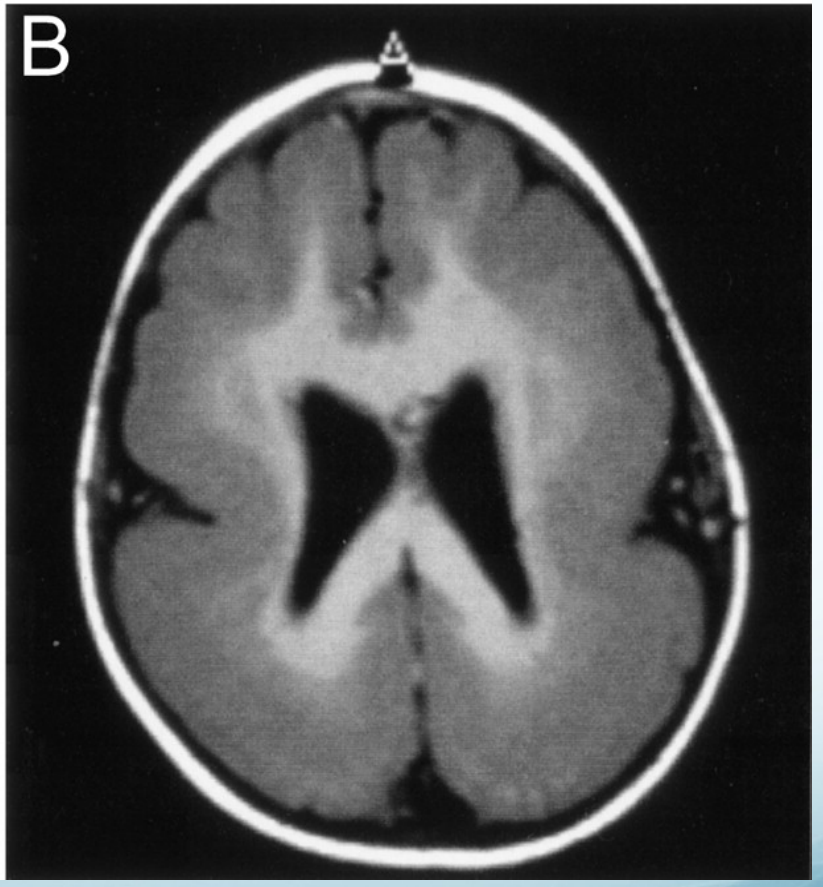


Pachygyria

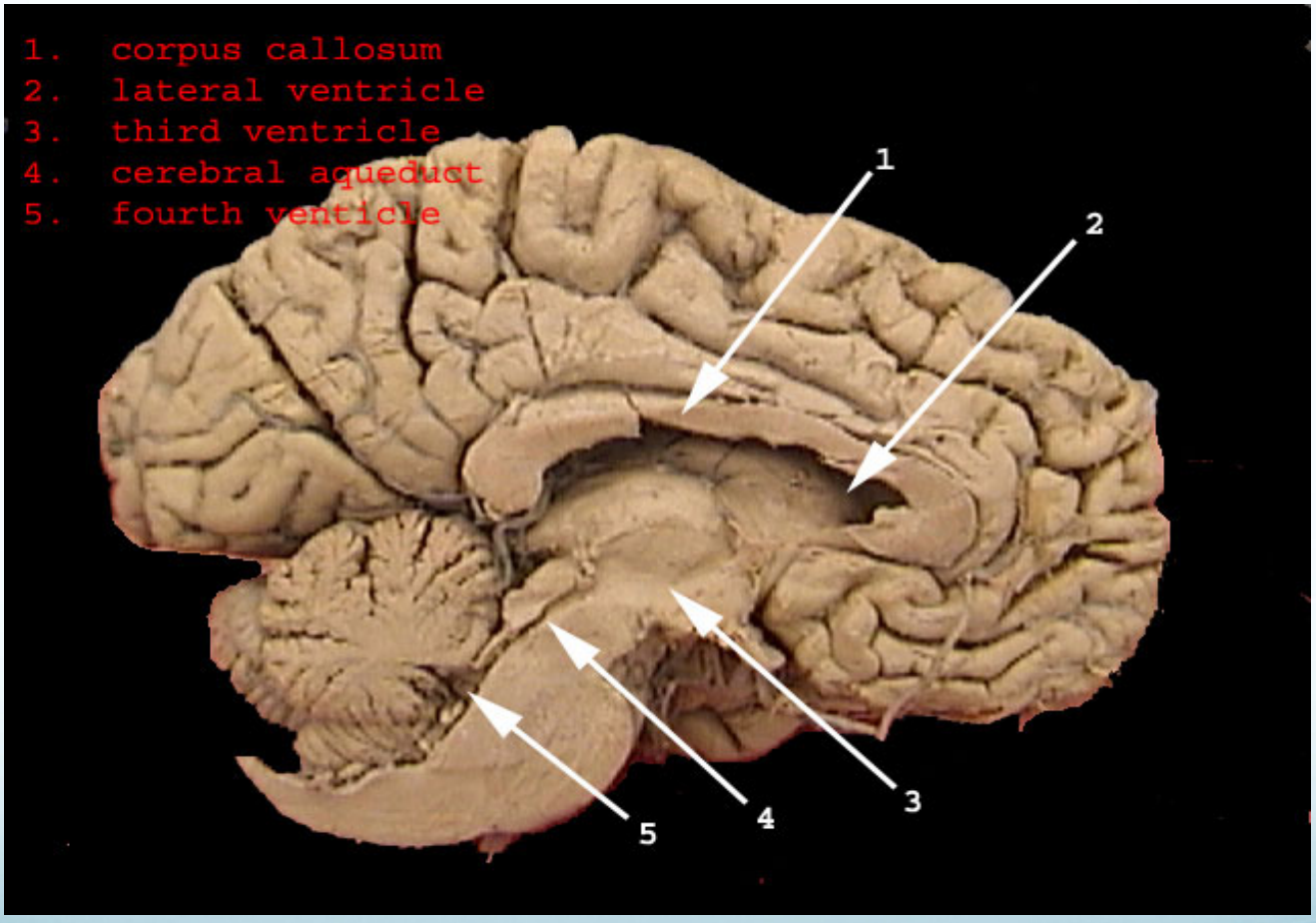
- Thickened abnormal cortex. Depending on extent, it may lead to cerebral palsy or to epilepsy.

Pachygyria





Agenesis of Corpus Callosum



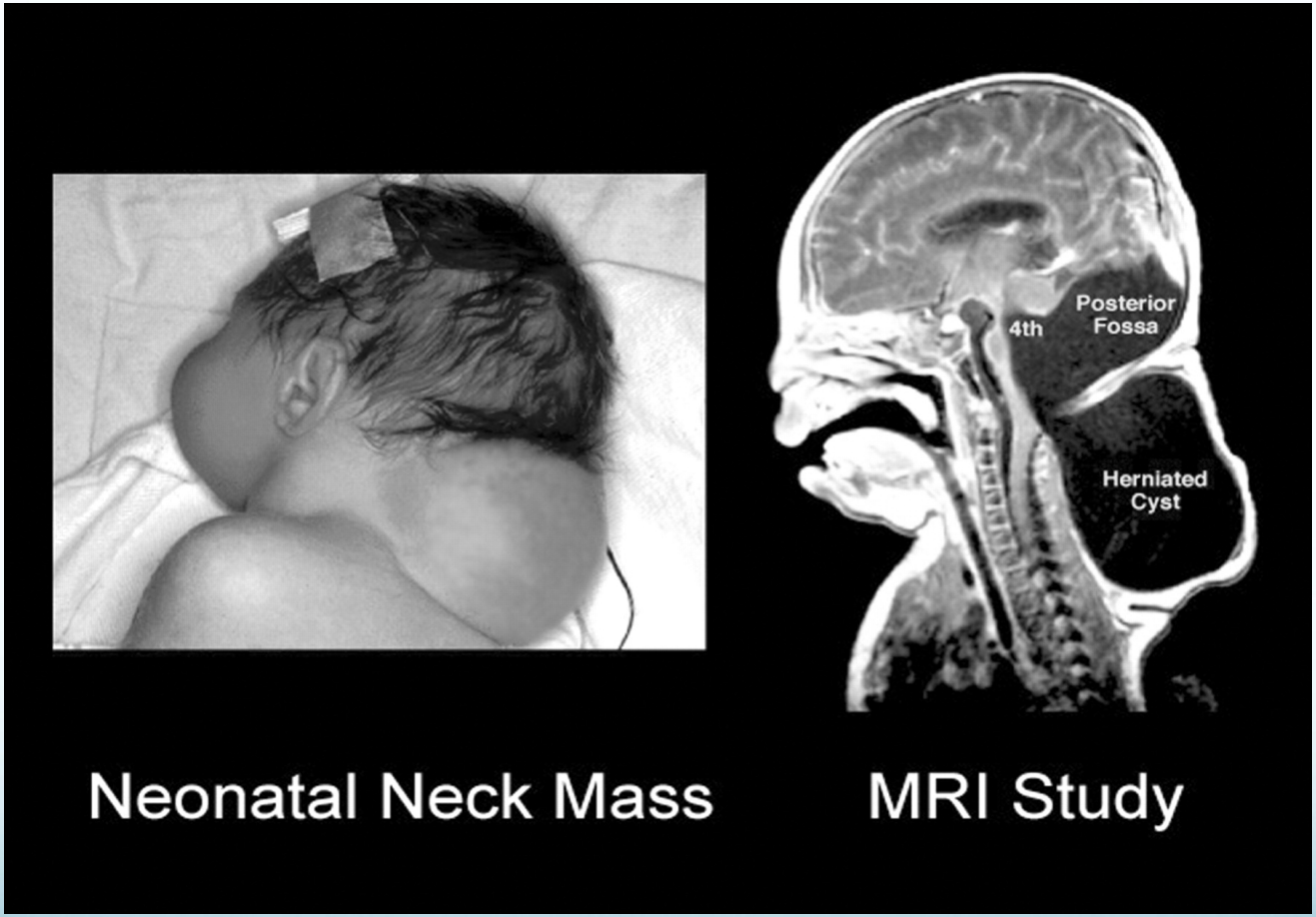
Agenesis of Corpus Callosum

- Corpus callosum develops between the 10th and 12th weeks of embryonic life. Agenesis may be isolated or associated with other malformations. Extent of other malformations determines disability.

Dandy-Walker malformation

- Classical Dandy-Walker malformation includes:
- Complete or partial agenesis of cerebellar vermis
- Large cystic formation in posterior fossa as a result of dilatation of fourth ventricle
- Hydrocephalus, which may not develop until adulthood.
- May be associated with other cerebral malformation;
- Considered part of a continuum including Dandy-Walker variant (part of vermis present, posterior fossa not enlarged) and megacisterna magna (complete vermis, large retrocerebellar cyst).

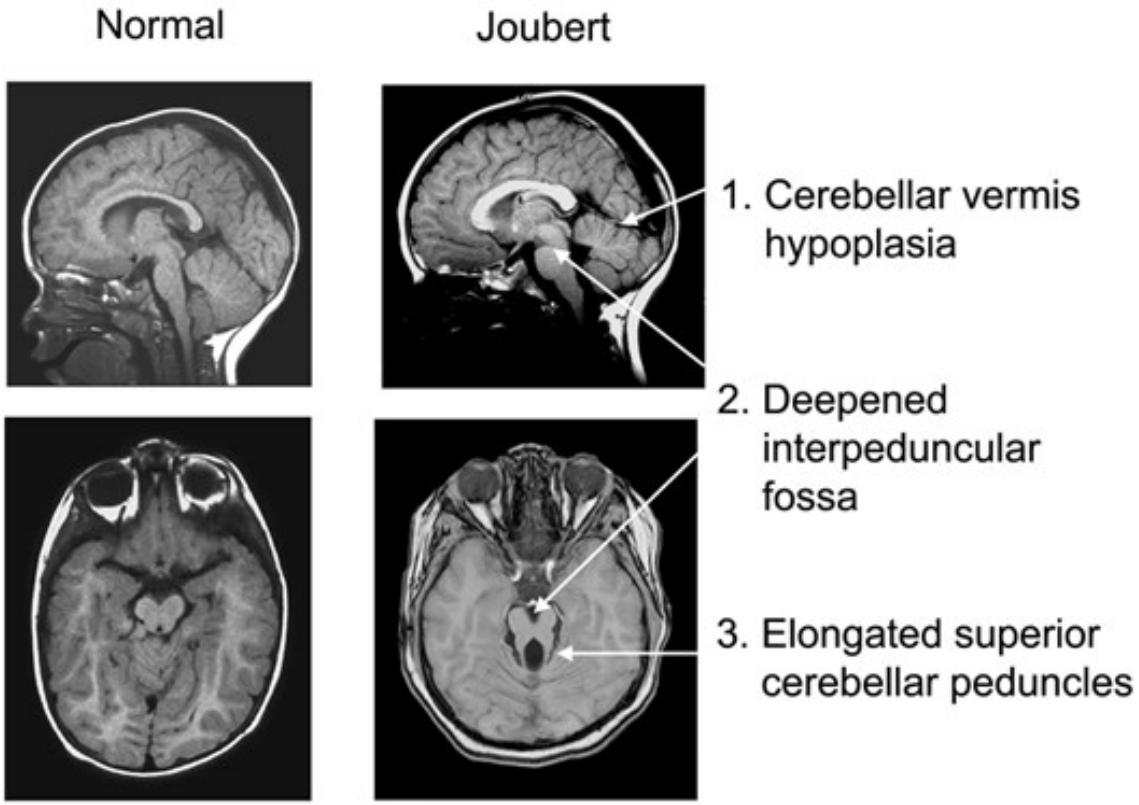
Dandy-Walker malformation



Joubert Syndrome

- Familial agenesis of cerebellar vermis, associated with episodic hyperpnoea, ataxia and cognitive impairment.

Joubert Syndrome



Aqueduct stenosis

- Cause of hydrocephalus in 11% of cases. Aqueduct may be reduced in size or may be represented by numerous channels within aqueduct location. Can occur in X-linked syndrome.

Neonatal Neurology

- **Neonatal Seizures:** Seizures are a major neurological problem in the first 28 days of life.
- **Classification:**

- Tonic
- Multifocal clonic
- Focal clonic
- Subtle
- Myoclonic

Neonatal Seizures

- **Causes:**
- Hypoxic-ischaemic encephalopathy
- Intracranial haemorrhage
- Intracranial infection
- Cerebral malformations
- Metabolic disturbances
- Withdrawal seizures
- Familial neonatal convulsions

Hypoxic-ischaemic encephalopathy

- The neonatal brain is highly resistant to hypoxia-ischaemia compared with that of an adult. The degree of hypoxia-ischaemia necessary to damage the neonatal brain usually leads to impairment of other organs.
- Hypoxia-ischaemia leads to depletion of brain phosphocreatine and ATP. Lactate increases.

Hypoxic-ischaemic encephalopathy

- **Clinical features:**
- Five-minute Apgar score of less than 6, a metabolic acidosis and hypotension are all suggestive of asphyxia in term infants.
- 3 Stages with different outcomes (80% die from stage 3)

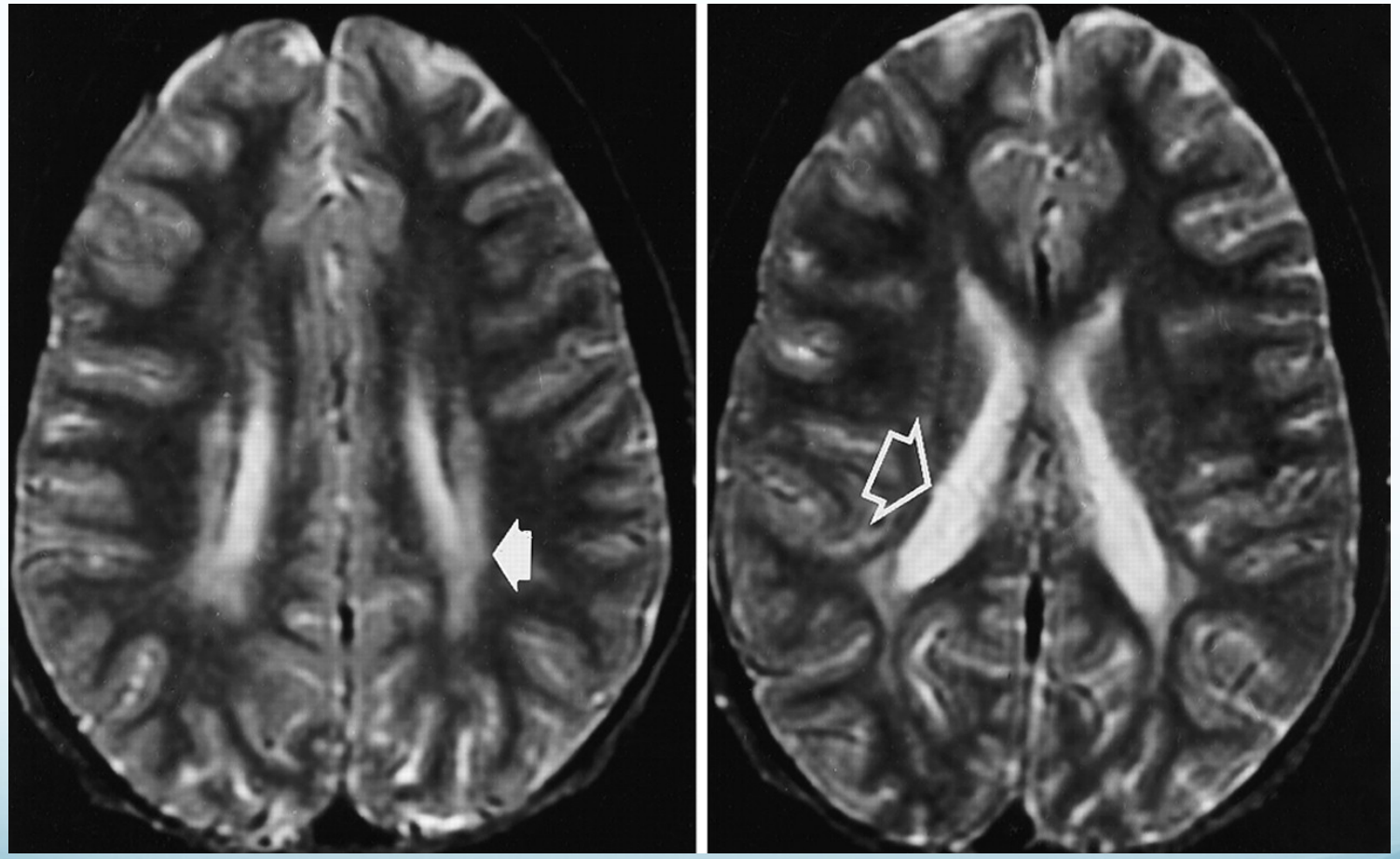
Periventricular-Interventricular Haemorrhage

- Usually a disease of preterm infants. Majority of haemorrhages originate in subependymal germinal matrix.
- Asymptomatic
- Catastrophic collapse
- Cerebral infarction
- Post-haemorrhagic hydrocephalus

Periventricular leukomalacia

- A pathological term to describe bilateral necrosis of periventricular white matter. Gliosis ensues. Leads to interruption of the fibres that are responsible for lower limb and optic function, so that periventricular leukomalacia is often the underlying pathology to the spastic diplegia and visual impairment seen in survivors of preterm birth.

Periventricular leukomalacia



Brachial plexus injuries

- Traction injury to the brachial plexus can follow difficulty in delivery of the shoulders and head during birth. A large baby, narrow birth canal and malpresentation may all contribute. Usually, the nerve roots are stretched but not completely avulsed. Clavicular or humeral fractures may also occur.

Erb's palsy

- C5-C6 lesion
- Affects deltoid, serratus anterior, supraspinatus, infraspinatus, biceps, brachioradialis muscles
- Arm is flaccid, adducted and internally rotated
- Elbow is extended, wrist is flexed ('waiter's tip')

Erb's Palsy



Klumpke's paralysis

- C8-T1 lesion
- Affects intrinsic hand muscles so that flexion of wrist and fingers is affected
- Cervical sympathetic involvement may lead to an ipsilateral Horner syndrome
- Physiotherapy
- Consideration of nerve root surgery

DISORDERS OF MOVEMENT

Cerebral palsy

- Cerebral palsy may be defined as a disorder of tone, posture or movement, which is the result of a static lesion affecting the developing nervous system. Despite the unchanging nature of the causative lesion, its existence in a developing nervous system means that its manifestations may change over time.
- Epidemiological studies suggest that at least 80% of cases of cerebral palsy are the result of prenatally acquired causes. A minority are the result of intrapartum asphyxia

Cerebral palsy

- **Classification:**
- **Spastic** (characterized by fixed increase in muscular tone)
 - Hemiplegia
 - Diplegia
 - Quadriplegia

Cerebral palsy

- **Athetoid** (dyskinetic, dystonic)
- Athetoid- writhing, involuntary pronation and flexion of distal extremity
- Choreiform ('dancing')- involuntary rapid semi-purposeful movements of proximal segments of body
- **Ataxic:** Mixed

Cerebral palsy

- Spastic diplegia is most frequently seen as the result of periventricular leukomalacia in preterm infants.
- Athetoid cerebral palsy may result from bilirubin encephalopathy or from brief profound anoxic-ischaemic episodes.

Cerebral palsy

- **Associated clinical features:**
- Developmental delay
- Tendency to joint contractures
- Epilepsy
- Perceptual difficulties
- Visual and hearing impairment
- Poor growth
- Feeding difficulties

Ataxia

- Acute cerebellar ataxia may occur following viral infection. It appears to be the result of both infectious and post-infectious processes; most commonly following varicella virus infection. Also measles, mumps, herpes simplex and Epstein-Barr viruses, coxsackie virus and echovirus.
- Occult neuroblastoma may also lead to acute ataxia.
- A common cause is over dosage of drugs such as carbamazepine, phenytoin, benzodiazepines. Also piperazine, antihistamines.

Ataxia

- **Other cause:**
- Posterior fossa tumour
- Migraine
- Ataxia Telangiectasia

Friedreich's ataxia

- Classified as a spinocerebellar degeneration
- Autosomal recessive condition (9q13)
- Gene product frataxin
- Involved in modulation of mitochondrial function

Friedreich's ataxia

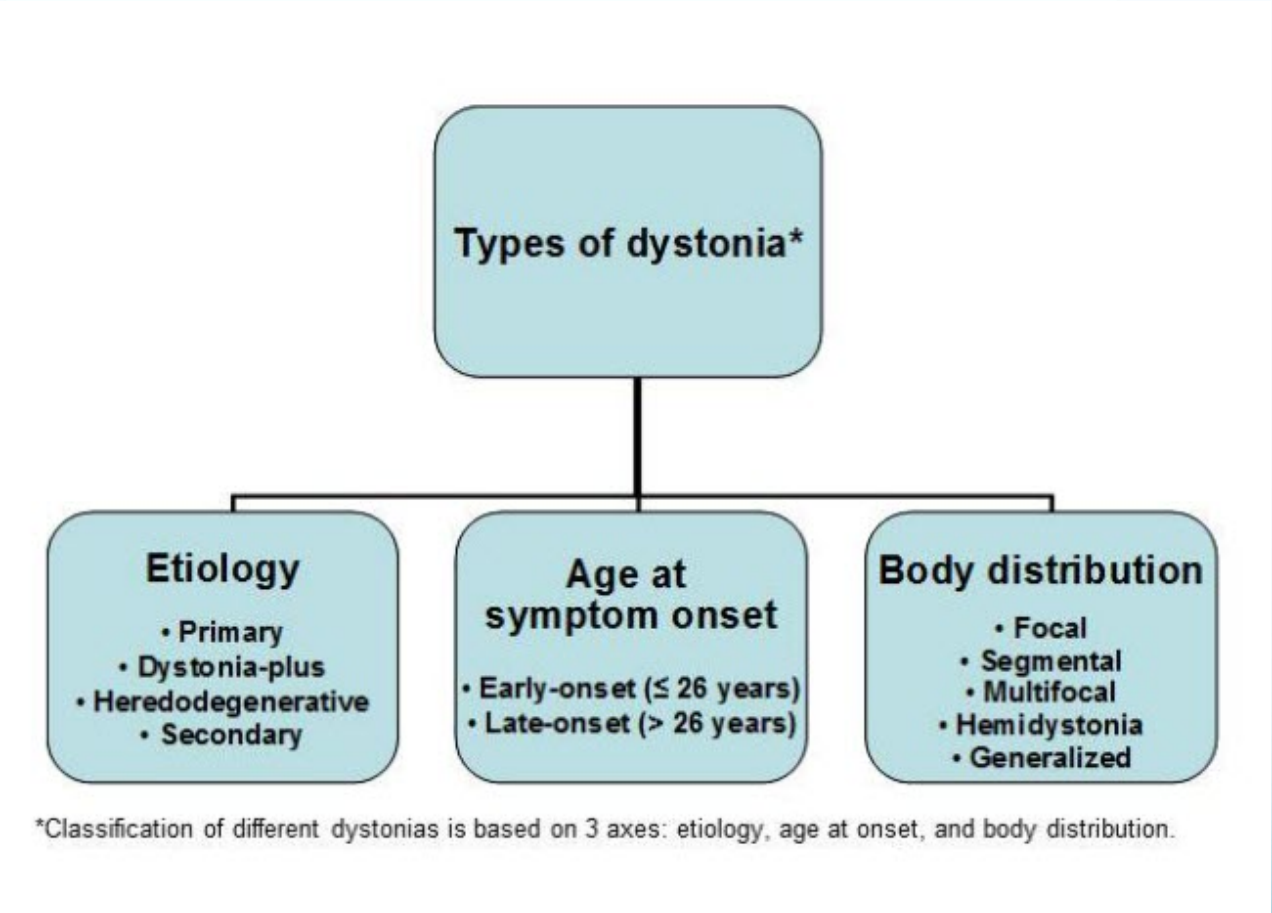
- Clinical characteristics:
- Onset of symptoms in first or second decade
- Loss of proprioception
- Increasing impairment of cerebellar function
- Development of pes cavus
- Cardiomyopathy develops
- Deterioration so that patients are usually not ambulant in their 20s or 30s

Friedreich's ataxia

- Treatment:
- Currently symptomatic
- Physiotherapy
- Suitable aids and appliances

Dystonia

- Definition: a condition in which muscle tone is abnormal without pyramidal involvement.



*Classification of different dystonias is based on 3 axes: etiology, age at onset, and body distribution.



Torsion Dystonia

- **Dystonia musculorum deformans**
- Genetically determined
- Autosomal dominant with incomplete penetrance
- Gene maps to **9q34** in Jewish families
- Other unidentified gene responsible in some non-Jewish families

Torsion Dystonia

- Clinical characteristics:
- Onset usually after **5** years
- May be focal or generalized
- Dystonia may be task-specific, for example, affected children may not be able to walk forwards but can walk backwards normally
- Often has gradual spread to other parts of the body
- Wilson disease should always be excluded
- Treatment: High-dose anticholinergic drugs
- Occasionally L-dopa

Dopa-responsive dystonia

- Described by Segawa
- Idiopathic dystonia
- Symptoms vary throughout the day
- Onset may be in the first 5 years
- Gene maps to 14q22.1 -q22.2
- Symptoms respond dramatically to low-dose L-dopa, which should be continued for life

Tics, Tourette syndrome

- Tics are involuntary movements affecting specific groups of muscles so that that the affected individual appears to have brief purposeless movements or actions. Tics may be motor or vocal.

Tics, Tourette syndrome

- **Simple tics:**
- Commonly affect children for a few months in mid-childhood
- Up to **25%** of children
- Spontaneous resolution
- **Multiple tics:**
- Some children are prone to tics of different types
- Different motor tics, vocal tics
- May not remit entirely

Tourette syndrome

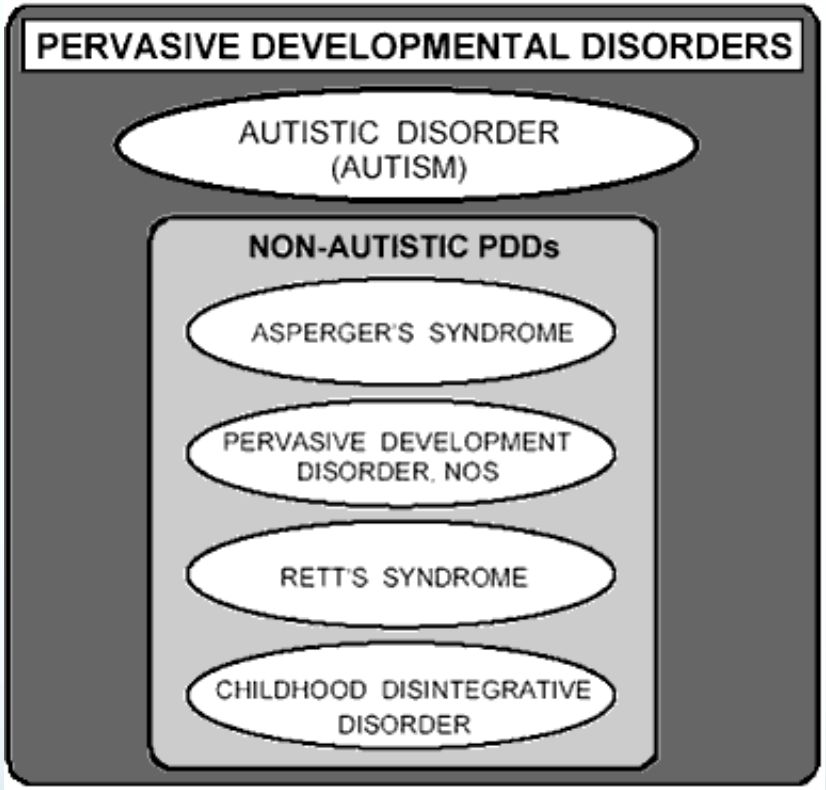
- This is defined by:
- Multiple motor tics
- One or more vocal tics
- Onset before 21 years of age
- Duration of > 1 year
- There is probably a continuum between multiple tics and Tourette syndrome.

Tics, Tourette syndrome

- **Other characteristic features of Tourette syndrome:**
- Echolalia (compulsive repetition of words or phrases just heard)
- Coprolalia (compulsive swearing)
- Attention-deficit disorder and obsessive compulsive features are present in 50%
- **Treatment**
- Tics may respond to haloperidol.

DEVELOPMENTAL DISABILITIES

Pervasive Developmental Disorders



Adapted for the web from: Shore, S. (2003). Beyond the Wall: Personal Experiences with Autism and Asperger Syndrome. 2nd Ed. Shawnee Mission, Autism Asperger Publishing Company. p. 158. Developed from: Siegel, B. (1996). The world of the autistic child: Understanding and treating autistic spectrum disorders. New York: Oxford Press.

Autism

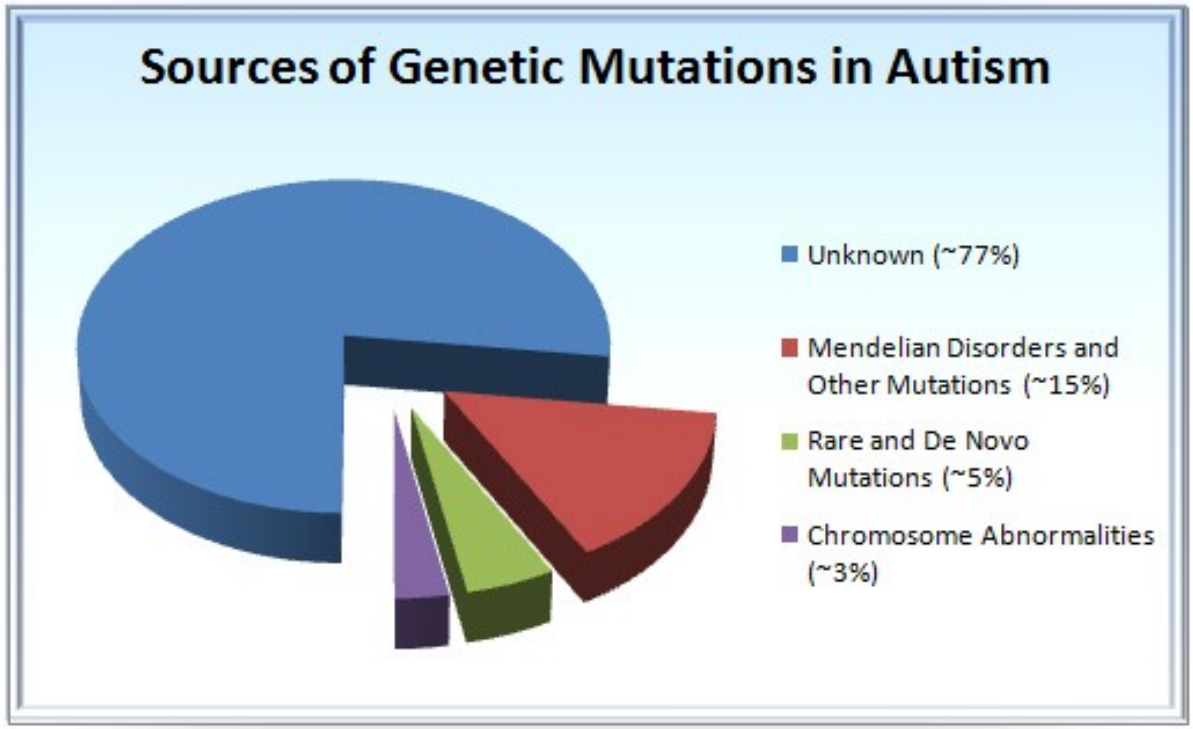


Always
Unique
Totally
Interesting
Sometimes
Mysterious

Autism

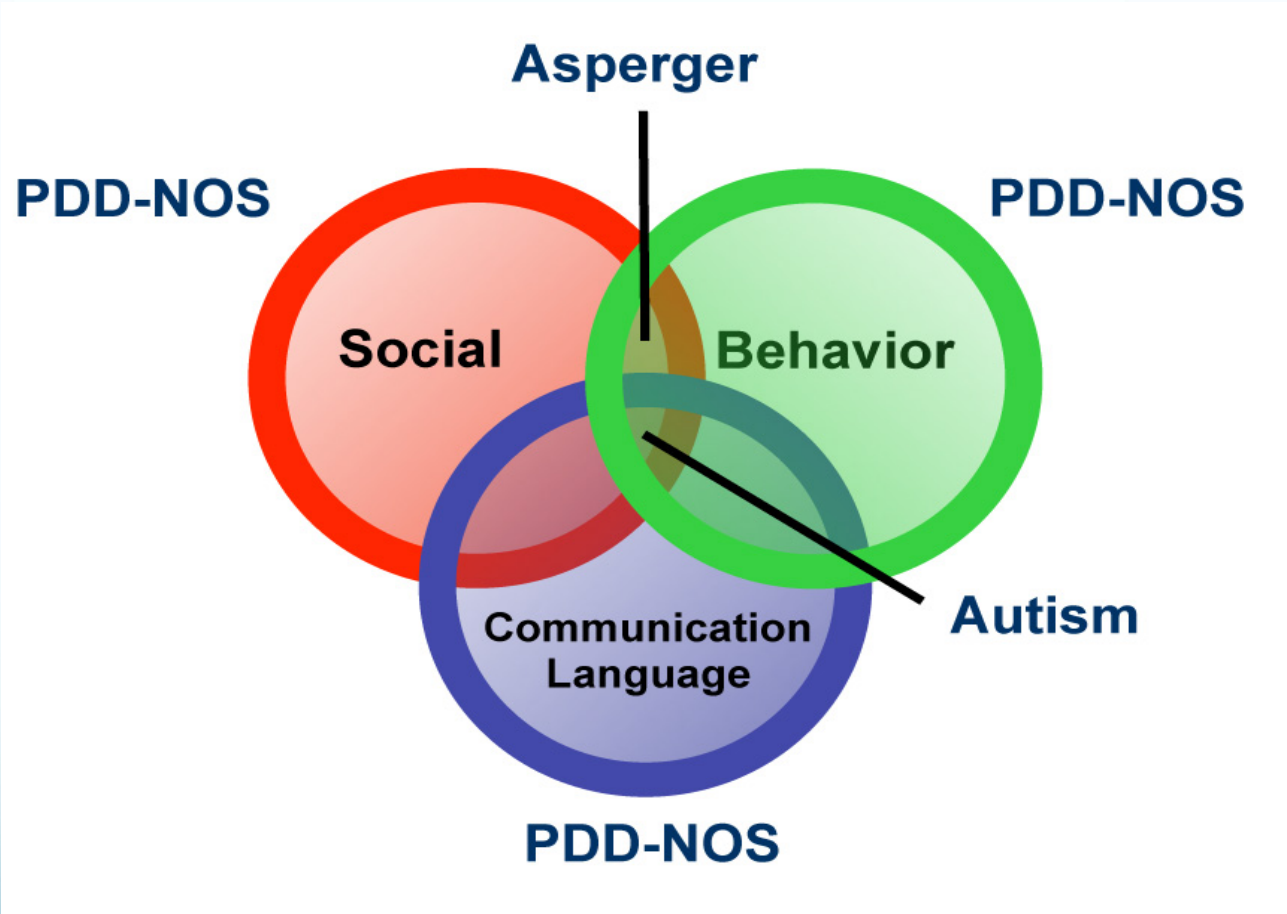
- Disturbance of reciprocal social interaction
- Disturbance of communication (including language, comprehension and expression)
- Disturbance of behaviour, leading to restriction of behavioural range

Autism

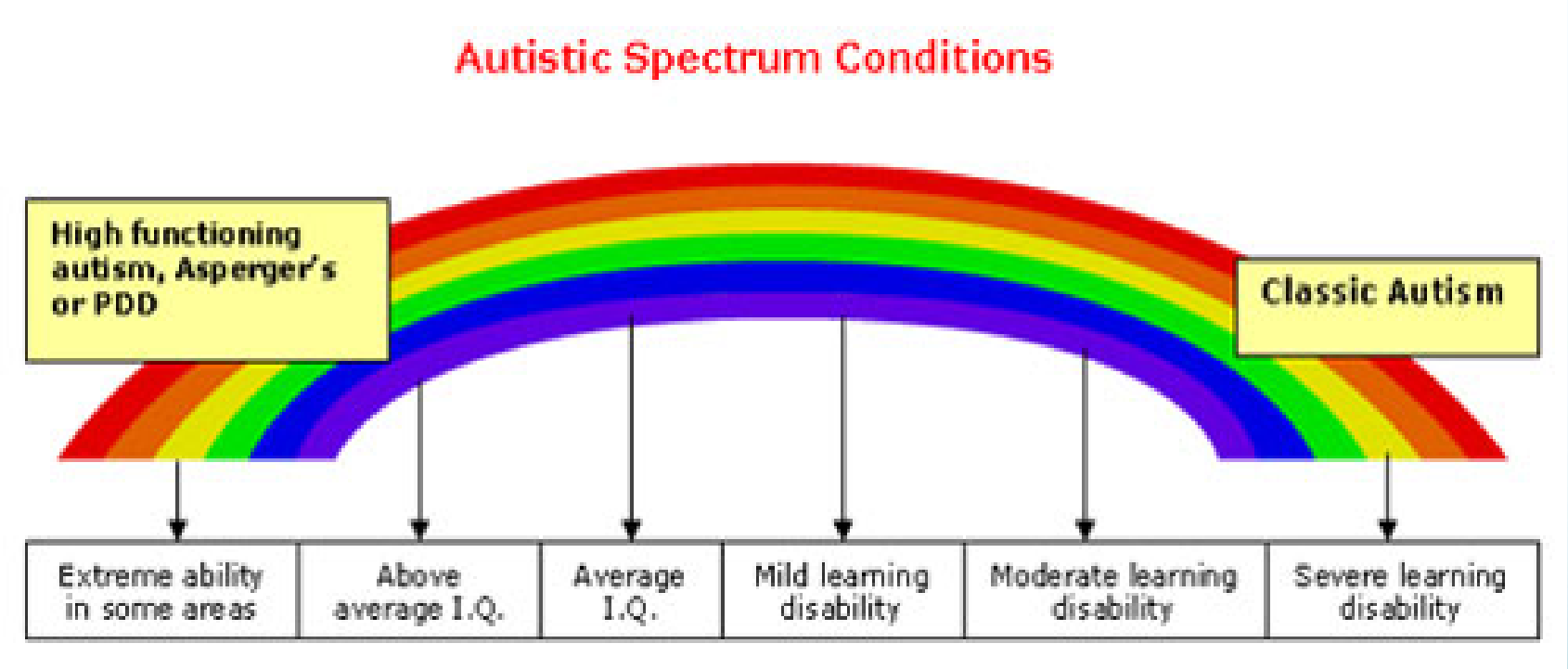


Data Source: Guo H, Hu Z, Zhao J, et. al. Genetics of Autism Spectrum Disorders. J Cent South Univ (Med Sci). 2011, 36 (8):703-711.

Autism

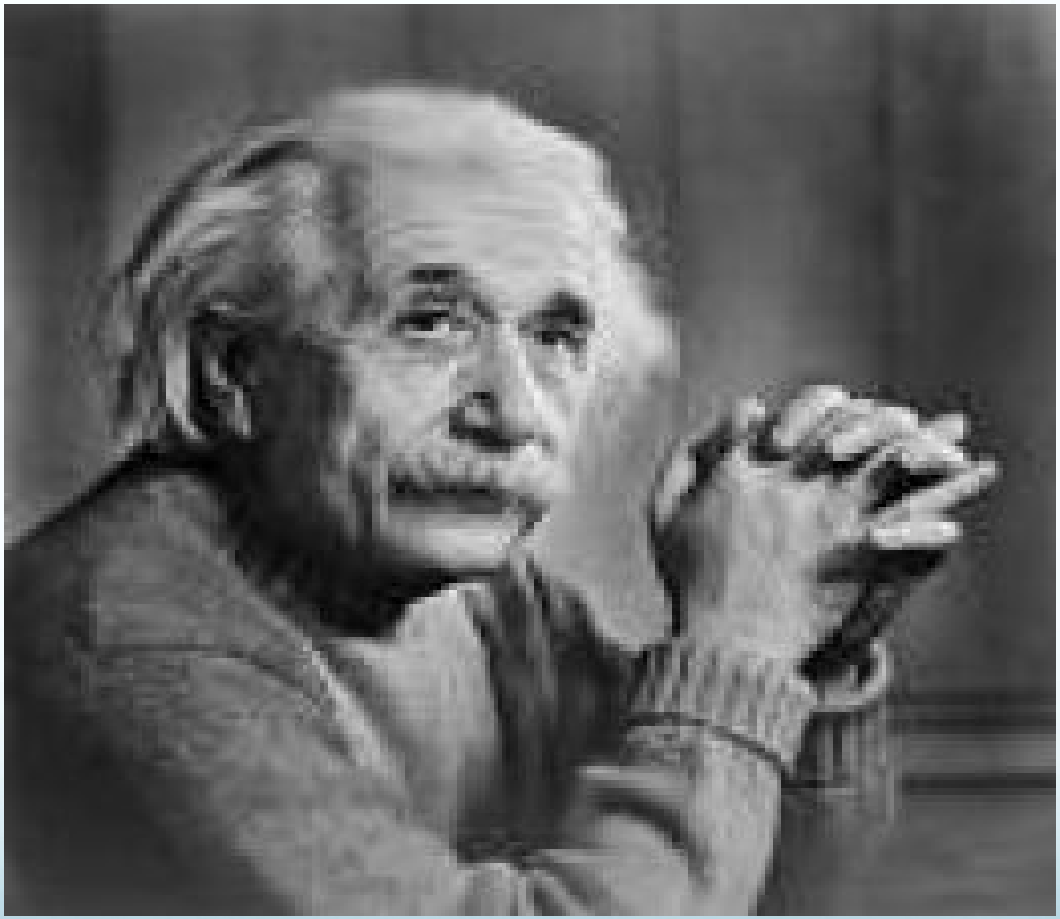

Asperger
PDD-NOS
PDD-NOS
Social
Behavior
Communication
Language
Autism
PDD-NOS

Autism

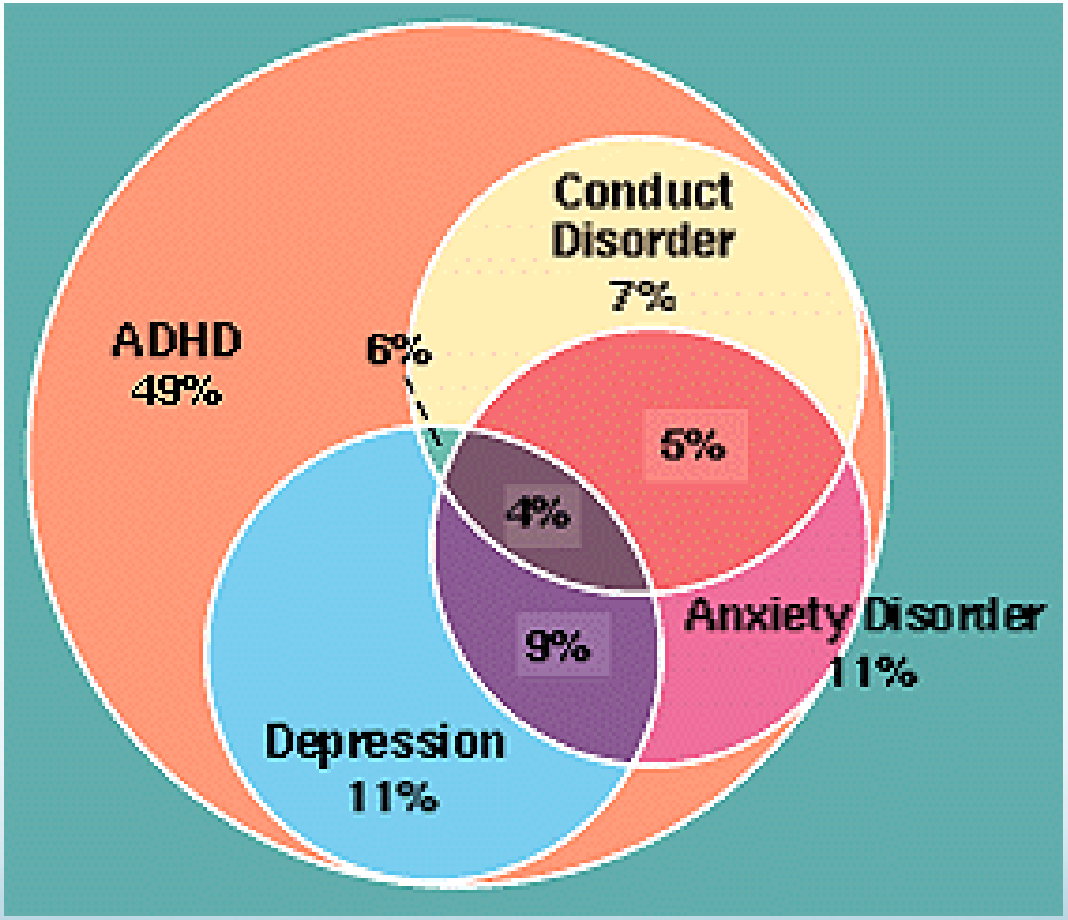

Autistic Spectrum Conditions
High functioning autism, Asperger's or PDD
Classic Autism
Extreme ability in some areas
Above average I.Q.
Average I.Q.
Mild learning disability
Moderate learning disability
Severe learning disability

Asperger syndrome

- Often considered to be on the autistic spectrum. It is characterized by autistic features in individuals of otherwise normal intelligence.
- Specifically characterized by:
- Impairment in social interaction
- Stereotypic behaviour
- No specific impairment of language



Attention-Deficit Hyperactivity Disorder

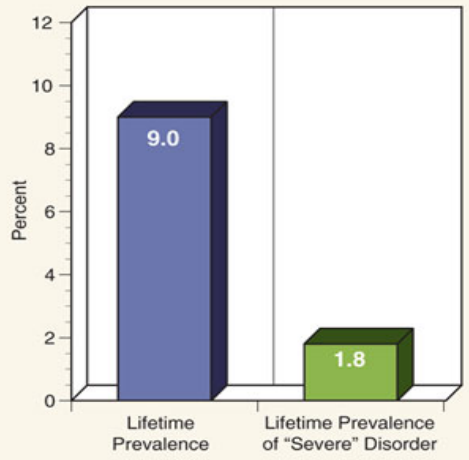


Attention-Deficit Hyperactivity Disorder

Attention Deficit Hyperactivity Disorder

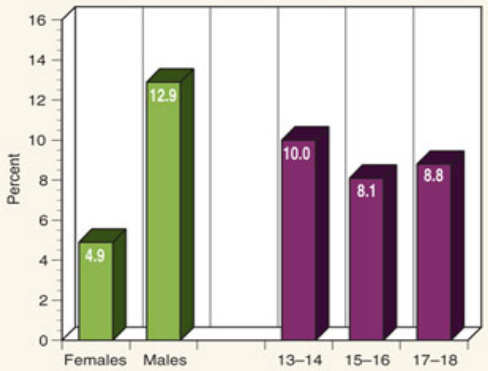
Lifetime Prevalence of 13 to 18 year olds

- **Lifetime Prevalence:** 9.0% of 13 to 18 year olds
- **Lifetime Prevalence of "Severe" Disorder:** 1.8% of 13 to 18 year olds have a "severe" disorder



Demographics (for lifetime prevalence)

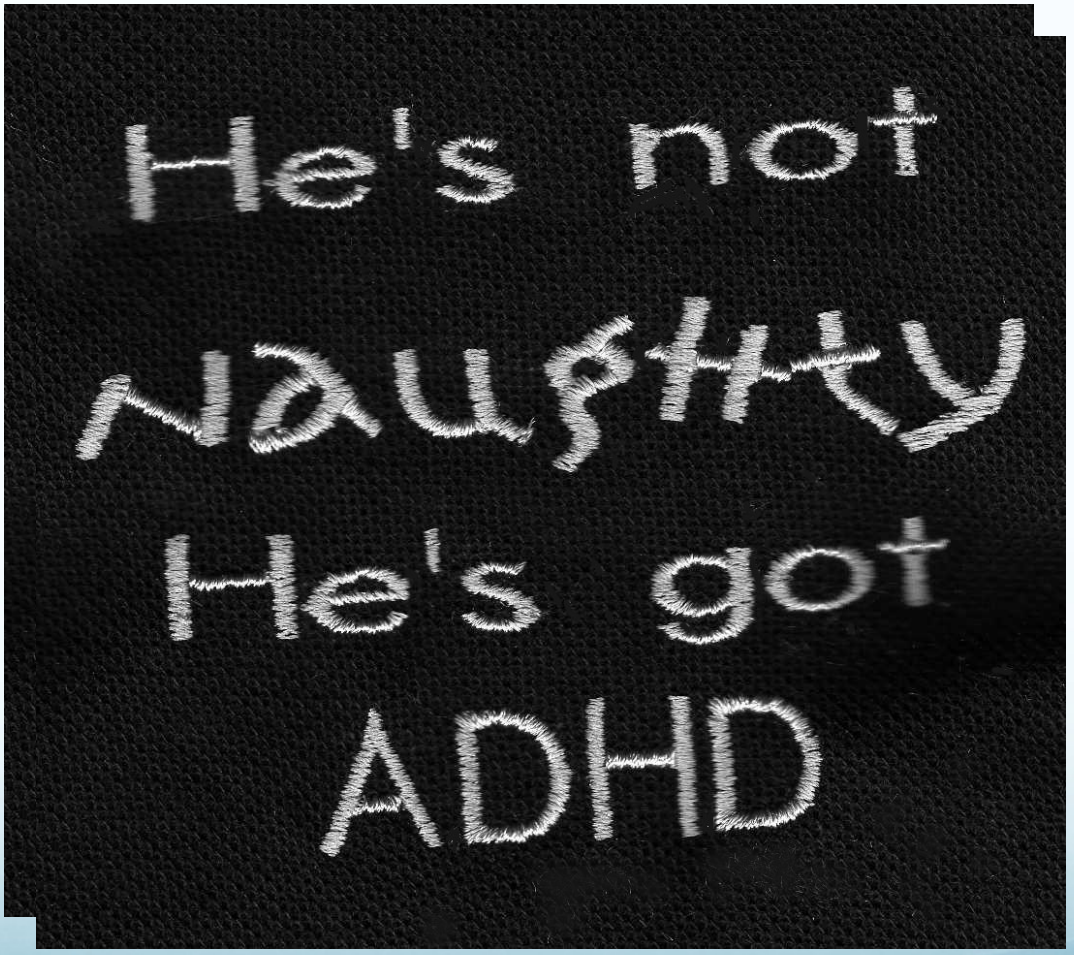
- **Sex and Age**



- **Race:** Not Reported

Merikangas KR, He J, Burstein M, Swanson SA, Avenevoli S, Cui L, Benjet C, Georgiades K, Swendsen J. Lifetime prevalence of mental disorders in U.S. adolescents: Results from the National Comorbidity Study-Adolescent Supplement (NCS-A). *J Am Acad Child Adolesc Psychiatry.* 2010 Oct;49(10):980-989.

Attention-Deficit Hyperactivity Disorder



Deficits in Attention, Motor control and Perception (DAMP)

- Often described as 'minimal brain damage' in the older literature
- Deficit in motor control and perception is often referred to as 'dyspraxia'
- Children have difficulties as described in varying degrees
- Treatment needs to include not only assessment but also educational help and a physical programme (occupational therapy)

EPILEPSY

- **Diagnosis:**
- Diagnosis of 'fits, faints and funny turns' is based primarily on clinical assessment of such events with recognition of characteristic patterns, supported by the results of special investigations.

EPILEPSY

- **Definition:**
- Epileptic seizures are clinical events which result from abnormal, excessive electrical discharge from cerebral neurones.
- Epilepsy is the tendency to have recurrent, usually unprovoked, epileptic seizures.

EPILEPSY

- **Classification:** The classification of epilepsy can be approached from the viewpoint of the characteristics of individual seizures or by identification of epileptic syndromes.
- Read carefully the classification page no 577,578

EPILEPSY

- **Generalized Epilepsy:**
- **Absence seizures:** Typical absence seizures - previously termed petit ma1 epilepsy, are characterized by brief (5-20 seconds) episodes of staring during which the child is unaware of his surroundings. Associated with 3-Hz spike and wave discharge on electroencephalogram (EEG). Can be precipitated by hyperventilation. Drugs of choice are sodium valproate, ethosuximide, lamotrigine.
- Atypical absences - EEG shows pattern of different frequency.

EPILEPSY

- **Myoclonic seizures:** Brief sudden generalized muscular jerks. Drugs of choice are sodium valproate, benzodiazepines, lamotrigine. May be exacerbated by carbamazepine.

- **Infantile spasms:** Onset in first 12 months. Brief sudden muscular contractions resulting in extension or flexion of the body. Attacks occur in runs. Associated with disorganized **EEG** described as hypsarrhythmia, as well as developmental arrest or regression. May be idiopathic or symptomatic (causes include tuberous sclerosis, perinatal hypoxic-ischaemic injury, inborn errors of metabolism). Treatment of choice is corticosteroids (or adrenocorticotropic hormone) or vigabatrin.

EPILEPSY

- **Juvenile myoclonic epilepsy:**
- Onset in adolescence - myoclonic seizures on wakening from sleep. Treatment of choice is sodium valproate; carbamazepine may exacerbate seizures.

EPILEPSY

- **Partial epilepsies:**
- **Benign childhood epilepsy** with centrotemporal spikes 'benign Rolandic epilepsy'. Characterized by predominantly nocturnal partial seizures with a slight male preponderance. Seizures may affect face or upper limbs; speech arrest may occur. Excellent prognosis for remission.

EPILEPSY

- **Complex partial seizures:** Characterized by stereotypic behaviour, loss of consciousness and focal EEG abnormalities.
- Often arise from temporal lobe foci. May respond to carbamazepine or sodium valproate.

EPILEPSY

- **Assessment:**
- Clinical picture
- ECG normal, sleep or sleep-deprived
- MRI

EPILEPSY

- **Management:**
- Explanation of potential risks and benefits of different therapies
- Medications start, depending on frequency and number of seizures
- Maintenance of seizure freedom with medication for perhaps 2 years
- Subsequent withdrawal of medication

EPILEPSY

- Some forms of partial epilepsy may be amenable to epilepsy surgery - when seizure disorder is intractable - site of seizure onset can be localized site is non-eloquent brain
- Other forms of treatment steroids, ketogenic diet, vagal nerve stimulation

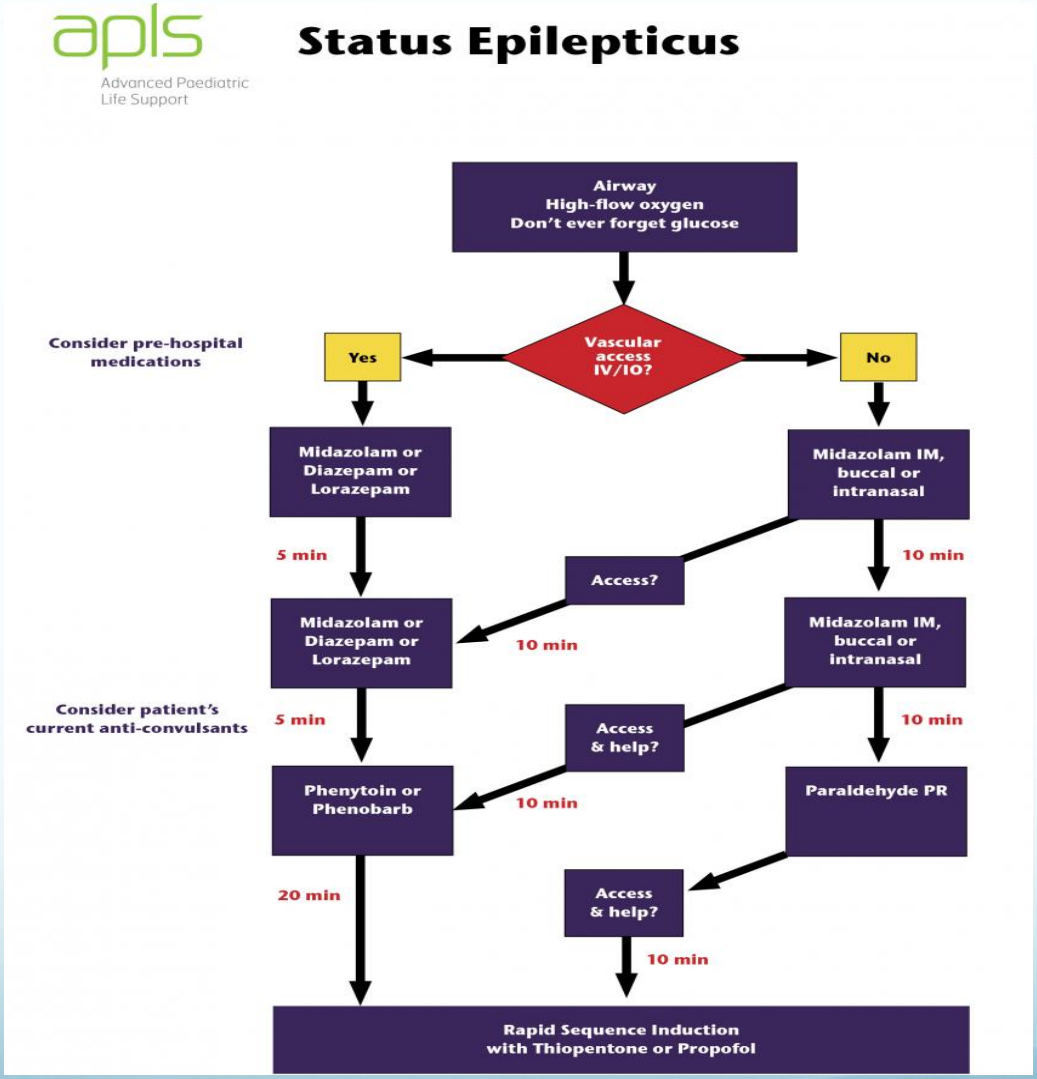
EPILEPSY

- **Anticonvulsant drugs:**
- Carbamazepine
- Sodium valproate
- Lamotrigine
- Vigabatrin
- Ethosuximide
- Gabapentin

EPILEPSY

- Oxcarbazepine
- Topirarmate
- Clobazam
- Clonazepam
- Phenytoin
- Phenobarbital
- Levetiracetam
- Tiagabine

Status Epilepticus



EPILEPSY

- **Prognosis:**
- *70%* of children with epilepsy are seizure-free by their 16th birthday.
- Remission is less likely in:

partial epilepsy, symptomatic epilepsy, some epilepsy syndromes such as juvenile myoclonic epilepsy or epileptic encephalopathies such as Lennox-Gastaut syndrome.

NON-EPILEPTIC SEIZURES

- **Anoxic Seizures:**
- **A) Breath-Holding attacks:**
- are seen in young children, often in the setting of a tantrum. The thwarted child screams and screams and holds his or her breath, becoming cyanosed and sometimes exhibiting subsequent convulsive movements. It may be possible to encourage the child to take a breath by gently blowing on his face. The tendency to have such episodes abates as children become older.

NON-EPILEPTIC SEIZURES

- **Anoxic seizures:**
- **B) Reflex anoxic seizures:** are the clinical manifestation of vagocardiac attacks. The precipitant may be a sudden, unexpected, painful stimulus or, occasionally, vomiting. Increased sensitivity of the vagus nerve leads to bradycardia, or even brief asystole, leading to pallor and cerebral anoxia-ischaemia. Following collapse, the child may then exhibit convulsive movements. Recovery is spontaneous. Apart from the risk of injury during a collapse, the prognosis is good with few, if any, individuals suffering adverse cerebral effects. The tendency to have such attacks improves with age but is often not completely abolished. Diagnosis can be confirmed by eliciting bradycardia under controlled monitoring conditions by exerting eyeball pressure.

NON-EPILEPTIC SEIZURES

- **Psychogenic seizures:** A small proportion of children have episodes of collapse, or even epileptiform attacks, which are under conscious or subconscious control. The trigger for these episodes is usually some form of psychological disturbance, which may be deeply hidden

- The nature and setting of the attack is often a clue to the event. The attack itself may include sudden collapse without, for example, pallor or an epileptiform attack, during which the child may respond to his surroundings. The setting of the attack is often to gain maximum attention for the episode. There is often some form of behavioural trigger to elicit an event.

NON-EPILEPTIC SEIZURES

- Prolonged EEC and electrocardiographic monitoring may be helpful in supporting the diagnosis and in helping families accept the nature of the attack.
- Management is via psychological or psychiatric treatment.

Headaches

- Headache is a common complaint in childhood. Population studies estimate that up to **35%** of children have complained of headache at some time. The commonest cause of headache in Western populations is tension or psychogenic headache.

Headaches

- Tension or psychogenic headache
- Migraine
- Vascular disorders
- Increased ICP
- Inflammatory disorders
- Referred Pain
- Miscellaneous

Tension headaches

- Often occur daily
- Generalized, dull-may involve band-like compression around head
- Worsens over the day
- Worse with stress
- Normal examination
- Anxious or depressed affect
- Depressive features in history

Tension headaches

- Reassurance
- Supportive psychotherapy

Migraine

- Defined as 'familial disorder characterized by recurrent attacks of headache widely variable in intensity, frequency and duration. Attacks are commonly unilateral and are usually associated with neurological and mood disturbance. All of the above characteristics are not necessarily present in each attack or in each patient'.

Migraine

- **Classification:**
- Common migraine (no aura)
- Classical migraine (aura preceding onset of headache)
- Complicated migraine (persisting neurological deficit after migraine attack)
- Basilar migraine
- Migraine variance
- Cluster headaches

Migraine

- **Treatment:**
- **Acute:** analgesics, relaxation, occasionally antiemetics
- **Prophylaxis:** avoidance of triggers such as cheese, pizotifen, propranolol

Brain Growth

- Brain growth is usually the most important determinant of head growth. In full-term infants, the rate of head growth is 2 cm per month in the first **3** months, in the second 3 months it is 1 cm per month and in the subsequent 6 months it is 0.5 cm per month.

Macrocephaly

- Familial macrocephaly
- Hydrocephalus
- Chronic subdural haematomata
- Associated disorders such as tuberous sclerosis or neurofibromatosis
- Metabolic conditions

Microcephaly

- Defined as occipitofrontal head circumference, below two standard deviations for age, sex and gestational age.
- **Causes:**
- Insults during pregnancy
- Perinatal insults
- Encephalopathies in infancy
- Autosomal recessive microcephaly

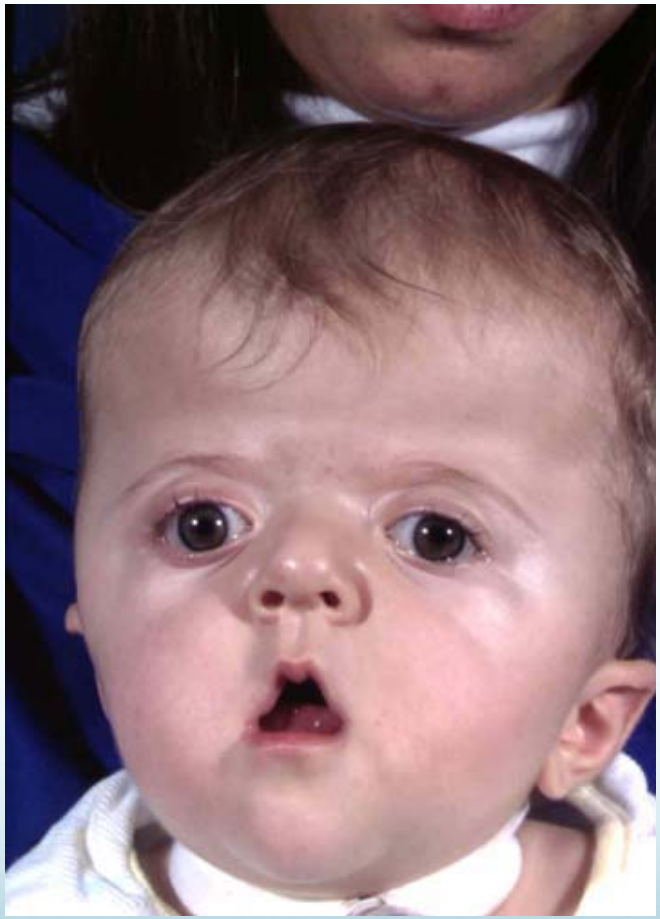
Microcephaly

- Chromosomes
- Antibodies to congenital infections
- Metabolic screen
- MRI scan
- Consider measurement of maternal plasma amino acids to exclude maternal phenylketonuria

Abnormal Head Shape

- Craniosynsotosis
- Scaphocephaly
- Dolicocephaly (sagittal suture)
- Brachcephaly (coronal suture)
- Plagiocephaly (unilateral premature closure of lambdoidal and coronal sutures)
- Trigonocephaly (metopic suture)
- Oxycephaly (acrocephaly) (fusion of coronal and lambdoidal sutures)

Apart syndrome



- malformations of the skull, face, hands and feet
- AD
- Cardiac abnormalities: PDA, PA,

Crouzon syndrome



- craniofacial dysostosis
- caused by a mutation in the fibroblast growth factor receptor II, located on chromosome 10.
- Autosomal Dominant

Crouzon syndrome



The Floppy Infant

- General: Prematurity, Intercurrent illness, Ligamentous laxity
- Chromosomal: Down & Prader Willi syndrome
- Metabolic: aminoaciduria, organic aciduria
- Muscle: congenital muscular dystrophy, congenital myopathies and congenital myotonic dystrophy
- Spinal: cervical cord injury
- AHCs: Polio, Werdnig Hoffmann

The Floppy Infant

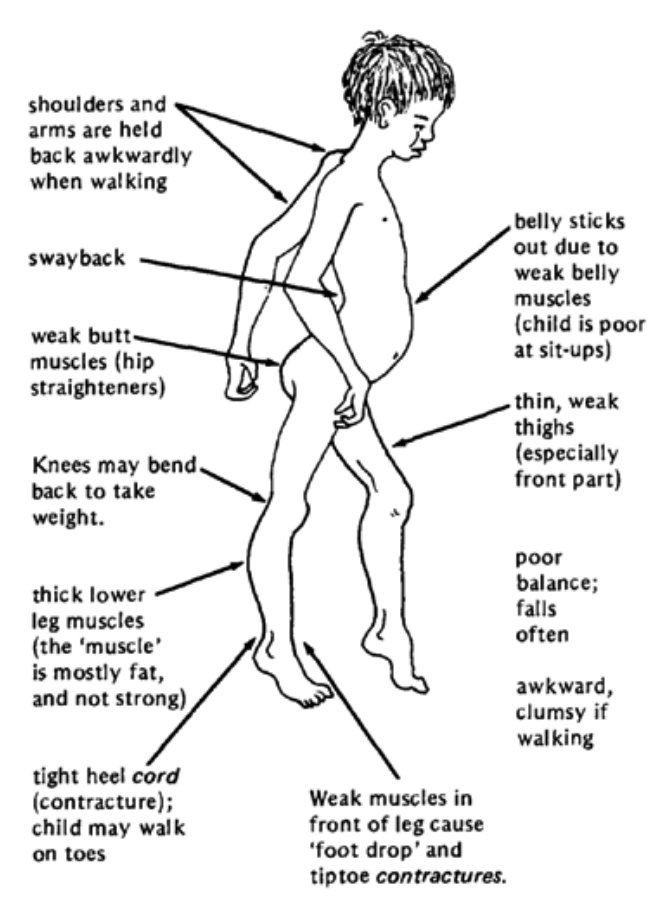
- Peripheral Neuropathy
- Neuromuscular junction: Transient myasthenia and congenital myasthenic syndrome

Duchenne muscular dystrophy

- X linked recessive
- 1:3500 male birth
- Female carriers are asymptomatic
- Caused by mutations in the dystrophin gene
- Gene comprises approximately 2 million base pairs
- Duchenne muscular dystrophy patients produce no dystrophin
- Becker muscular dystrophy (allelic, milder form) patients produce abnormal but
- functional protein Dystrophin is localized to muscle cell membranes

Duchenne muscular dystrophy

- Onset in early years
- Some cases are identified presymptomatically by abnormal transaminases measured during intercurrent illness
- Sometimes leads to faltering growth
- Early delay in motor milestones
- Difficulties in climbing stairs
- Lordosis with waddling gait


shoulders and arms are held back awkwardly when walking
swayback
weak butt muscles (hip straighteners)
Knees may bend back to take weight.
thick lower leg muscles (the 'muscle' is mostly fat, and not strong)
tight heel *cord* (contracture); child may walk on toes
Weak muscles in front of leg cause 'foot drop' and tiptoe *contractures*.
belly sticks out due to weak belly muscles (child is poor at sit-ups)
thin, weak thighs (especially front part)
poor balance; falls often
awkward, clumsy if walking

Duchenne Muscular Dystrophy

- Psuedohypertrophy of calves
- Progressive muscular weakness
- Tendency to joint contractures
- Typically, boys lose ability to walk between 8 and 12 years
- When dependent on wheelchair, boys are prone to develop scoliosis
- Respiratory failure supervenes

Gower Sign



Duchenne Muscular Dystrophy

- Increased incidence of learning disability
- Cardiomyopathy occurs
- Survival to late teens, early twenties

Duchenne Muscular Dystrophy

- High plasma creatine kinase (greater than 5000 lull)
- Mutations in dystrophin gene
- Muscle biopsy - dystrophic picture with absent dystrophin

Duchenne Muscular Dystrophy

- There is no curative treatment
- Physiotherapy
- Appropriate seating
- Management of scoliosis
- Non-invasive respiratory support
- Corticosteroids improve muscular power, but it is unclear as to when, how and for how long they should be administered

Becker Muscular Dystrophy

- Allelic disease to Duchenne muscular dystrophy
- Milder than Duchenne muscular dystrophy
- Patients walk beyond 16 years of age
- Similar clinical pattern to Duchenne muscular dystrophy
- Cramps can be problematical
- Prone to cardiomyopathy

Becker Muscular Dystrophy

- Duchenne and Becker muscular dystrophies are distinguished clinically and on muscle biopsy findings. Nature of genetic mutation can provide a pointer as to the severity of the condition but current routine genetic testing does not distinguish reliably between Duchenne muscular dystrophy and Becker muscular dystrophy; it just identifies a dystrophinopathy.

Emery-Dreifuss Muscular Dystrophy

- Uncommon X-linked muscular dystrophy (Xq28)
- Mild proximal muscular weakness
- Joint contractures
- Cardiac involvement: affected individuals may be prone to sudden cardiac death

Fascio-scapulohumeral Muscular Dystrophy

- Autosomal dominant muscular dystrophy **(4q35)**
- Facial, scapular and humeral wasting and weakness
- Slowly progressive Other muscles may be involved
- Variable expression within families

Limb-girdle Muscular Dystrophies

- Common on a world-wide basis
- May be inherited as autosomal dominant or autosomal recessive traits (at least three separate autosomal dominant and nine autosomal recessive limb-girdle muscular dystrophies have been identified so far)
- Variations in clinical phenotype
- Many are similar to Duchenne muscular dystrophy or Becker muscular dystrophy

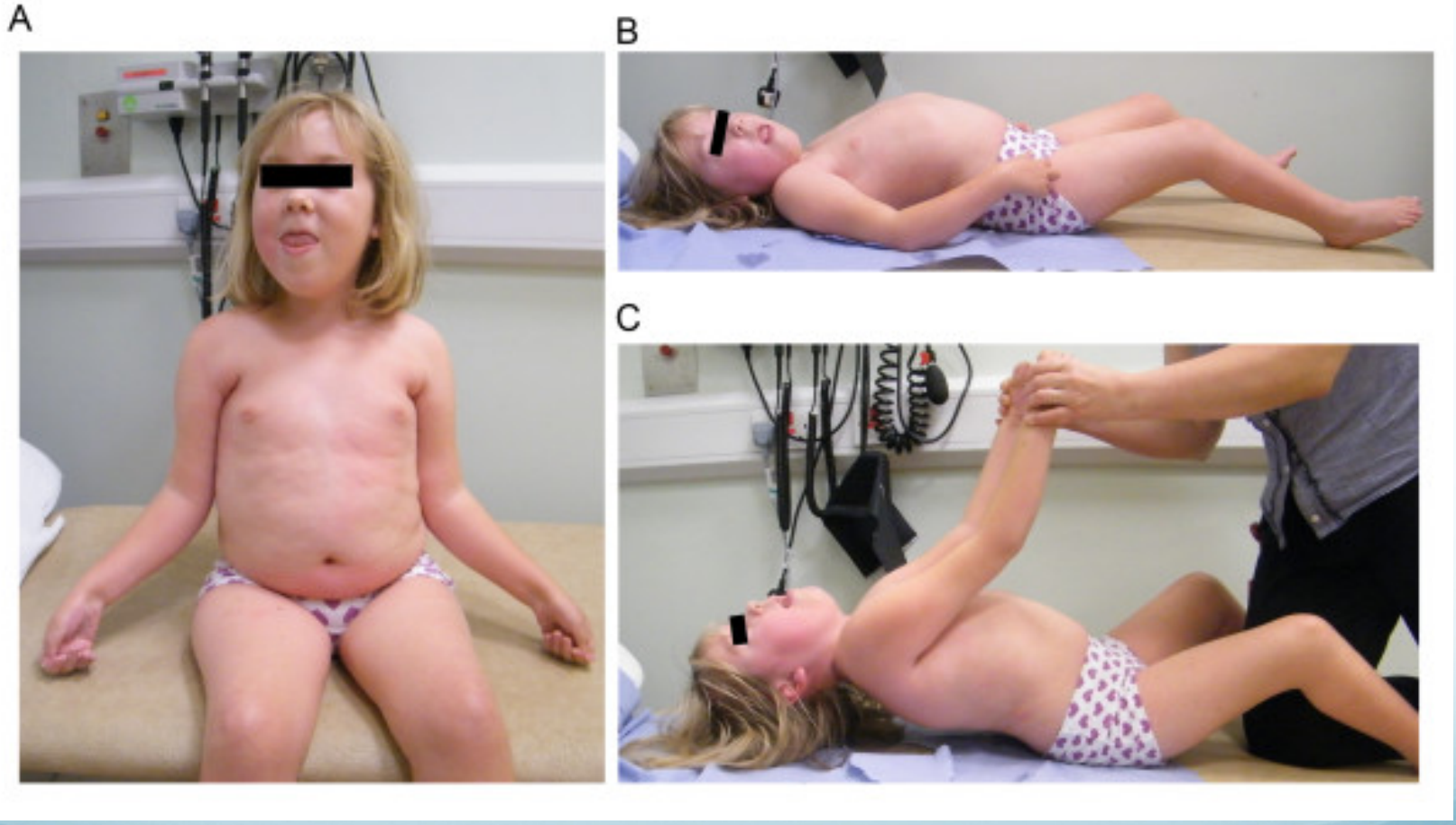
Congenital Muscular Dystrophies

- This is a group of disorders in infants characterized by muscular weakness, hypotonia and joint contractures from birth.
- Muscle biopsy shows typical dystrophic changes
- Different subtypes now being describe

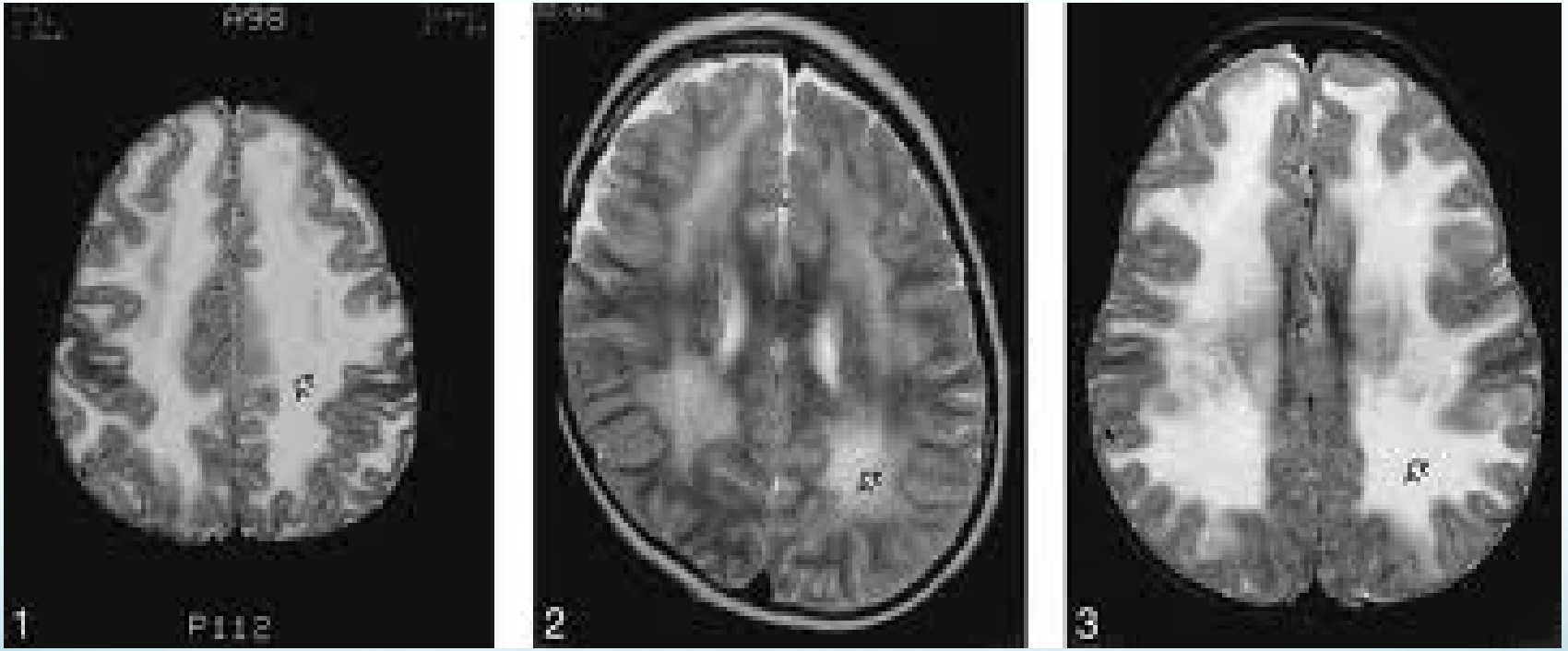
Merosin-negative congenital Muscular Dystrophy

- Characterized by absence of merosin on muscle biopsy
- Clinically hypotonia, weakness, contractures
- Often associated with learning disability
- Functionally, affected children do not achieve independent walking
- Autosomal recessive (6p2)

Merosin-negative Congenital Muscular Dystrophy



Merosin-negative Congenital Muscular Dystrophy



Merosin-positive Congenital Muscular Dystrophy

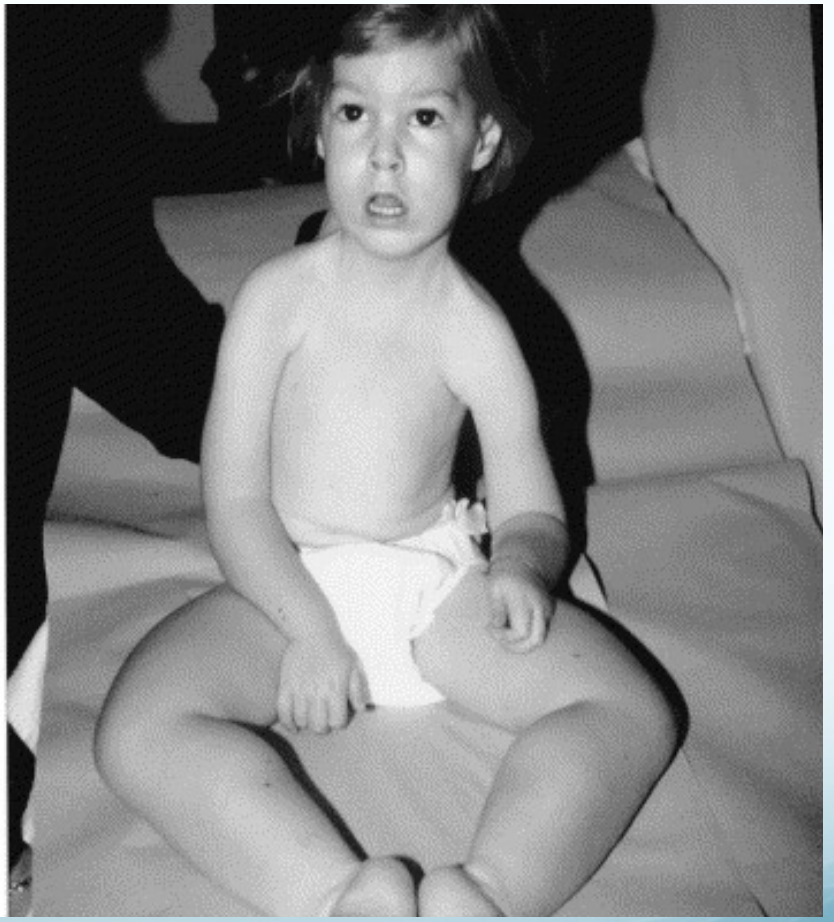
- Clinically less severe than merosin-negative congenital muscular dystrophy

Fukuyama congenital Muscular Dystrophy

- Autosomal recessive (9q31-q33)
- As well as severe weakness, affected individuals have brain malformations

Fukuyama congenital Muscular Dystrophy





Congenital Myopathies

- A group of disorders characterized by hypotonia and weakness from birth. Differentiated on clinical and histological features.
- Central cord disease
- Nemaline myopathy
- Myotubular myopathy

Myotonic Dystrophy

- Common (incidence 13.5 per 100,000 live births) neuromuscular condition. Autosomal dominant inheritance (19q13) Severity appears to be related to size of triplet repeat (CTG) in gene mutation

Congenital Myotonic Dystrophy

- Condition often unrecognized in mothers
- Preceding polyhydramnios
- Baby often born unexpectedly 'flat'
- Facial weakness, hypotonia
- Often requires respiratory support Joint contractures, especially talipes

Myotonic Dystrophy in older children and adults

- Facial weakness initially
- Then weakness affecting temporalis, sternomastoid, distal leg muscles
- Progressive weakness
- Difficulties in relaxing muscular contraction, e.g. difficulties in relaxing grip
- Cardiac involvement
- Gene mutation analysis
- Electromyogram in older children upwards (>3 to 4 years of age) shows characteristic ‘dive bomber' discharges

Myotonia Congenita (Thomsen disease)

- Rare
- Autosomal dominant inheritance
- Characterized by myotonia and cramps
- Muscular hypertrophy is typical

Myotonia Congenita (Thomsen disease)



Fig. 1 : Hypertrophy of thigh and calf muscles



Fig. 2 : Hypertrophy of biceps and forearm muscles



Fig. 3 : Percussion myotonia in thigh

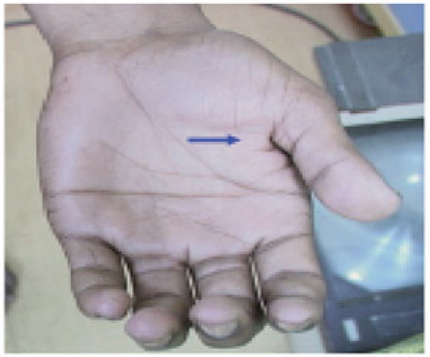


Fig. 4 : Percussion myotonia in thenar eminence

Anterior horn cell disease

- **Spinal muscular atrophy:** The spinal muscular atrophies are a group of heterogeneous conditions which are characterized by the clinical effects of anterior horn cell degeneration. The commonest in childhood are the autosomal recessive proximal spinal muscular atrophies.
- Absent deep tendon reflexes
- Symmetrical muscle weakness of trunk and limbs, more marked proximally than distally and in legs more than arms
- Tongue fasciculation. Investigations confirming neurogenic abnormalities

Spinal Muscular Atrophy:



Neuropathies

- Charcot-Marie-Tooth disease or peroneal muscular atrophy.
- AD, AR or X linked recessive

Charcot-Marie-Tooth Disease



Charcot-Marie-Tooth Disease



Guillain-Barre syndrome

- An acute demyelinating disease of peripheral nerves characterized by progressive weakness.
- Usually follows viral infection or immunization
- Numerous other infections, including *Campylobacterjejuni* gastroenteritis, have been implicated

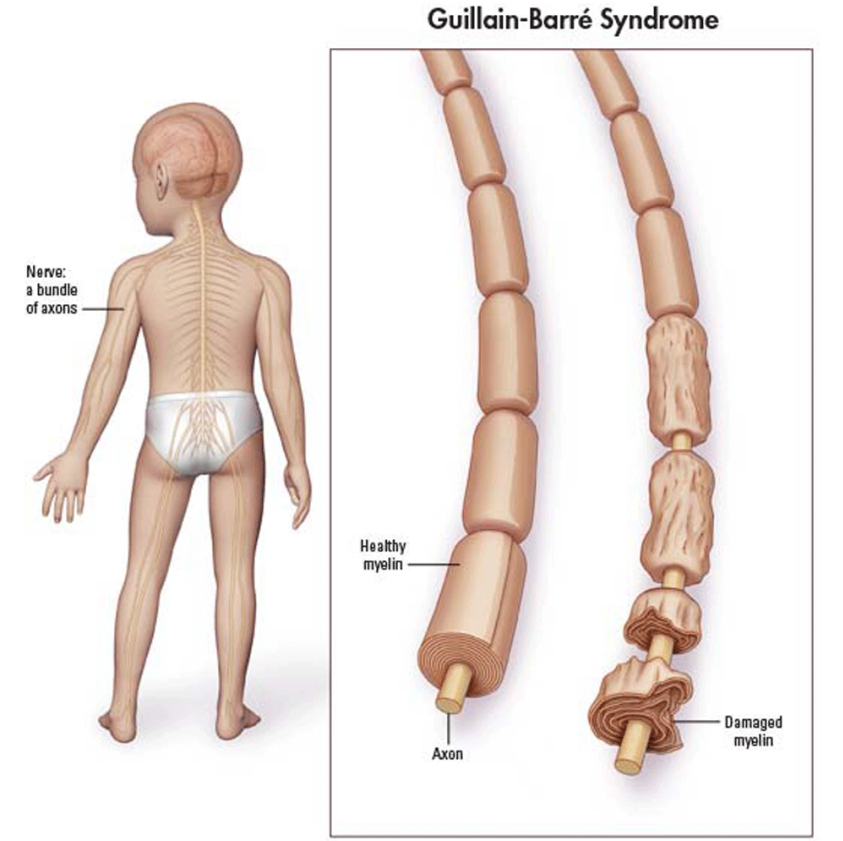
Clinical Features

- Sudden onset of weakness, usually affecting lower limbs
- Ascending paralysis
- Usually symmetrical weakness
- Pain often a prominent feature
- Sensory involvement in about 50%
- Respiratory muscle weakness may occur

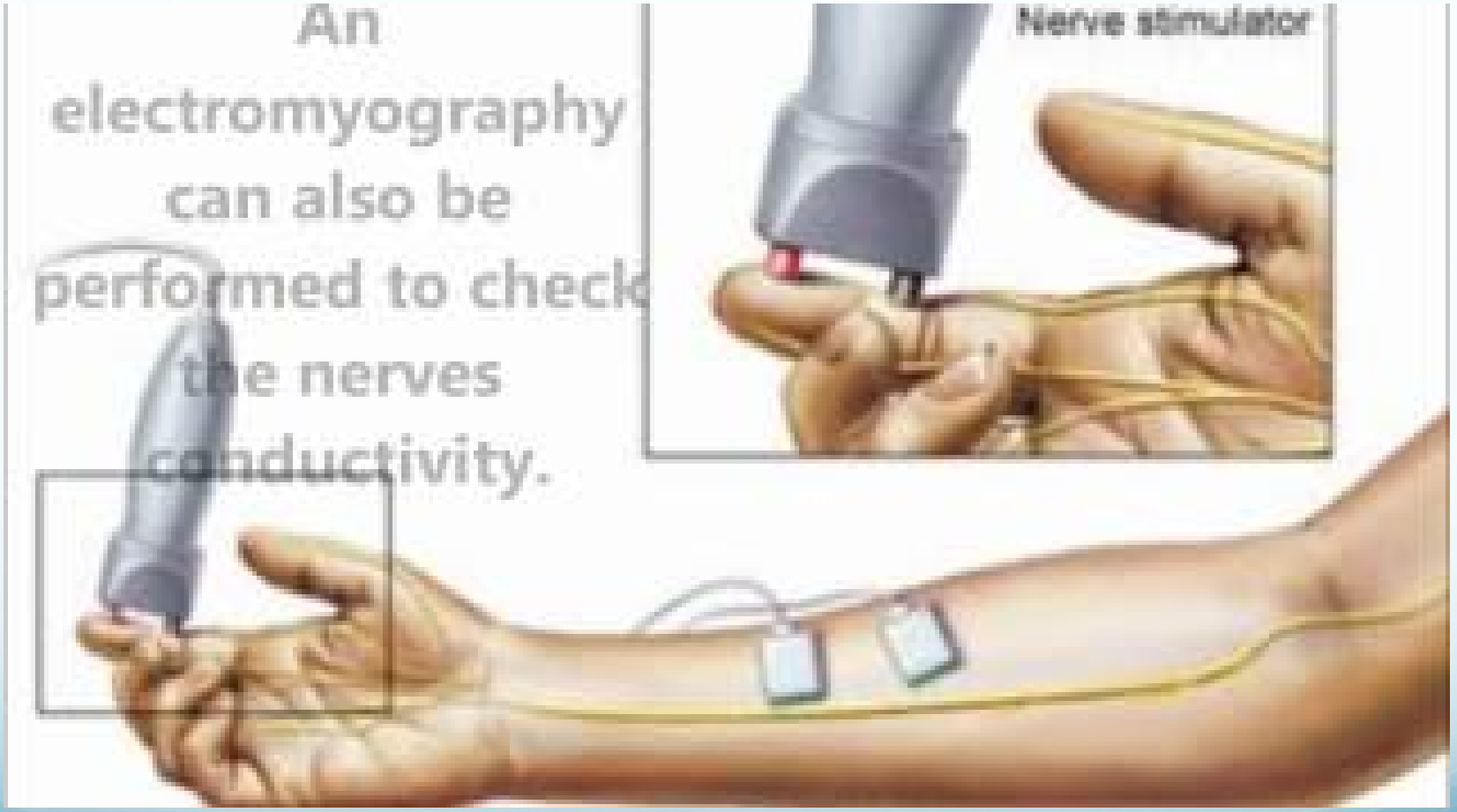
Diagnosis

- High CSF protein
- A marked slowing of motor neurone conduction velocity
- Conduction block

Diagnosis


Guillain-Barré Syndrome
Nerve:
a bundle
of axons
Healthy
myelin
Axon
Damaged
myelin

Diagnosis


An electromyography can also be performed to check the nerves conductivity.
Nerve stimulator

Course

- Deterioration over the first 10-20 days
- Plateau
- Recovery
- Mortality is 2-3% in children

Treatment

- Symptomatic
- Respiratory support
- Plasma exchange
- High-dose immunoglobulin

Juvenile Dermatomyositis

- A systemic illness affecting primarily the skin, muscles and gastrointestinal tract.
- Unlike adult dermatomyositis, juvenile dermatomyositis is not associated with malignancy.

Clinical Features

- Age of onset between 5 and 10 years
- May present with fever, muscle pain
- Onset can be insidious Increasing muscular weakness, mainly proximal
- Rash involving upper eyelids (heliotrope rash) and periorbital region develops
- Rash on extensor surfaces.
- Calcinosis is a feature
- May have difficulty swallowing
- Children are often miserable in advance of other symptoms

Dermatomyositis



Dermatomyositis



Diagnosis

- Creatine kinase may or may not be raised
- Muscle biopsy may show perifascicular atrophy, but changes can be patchy

Treatment

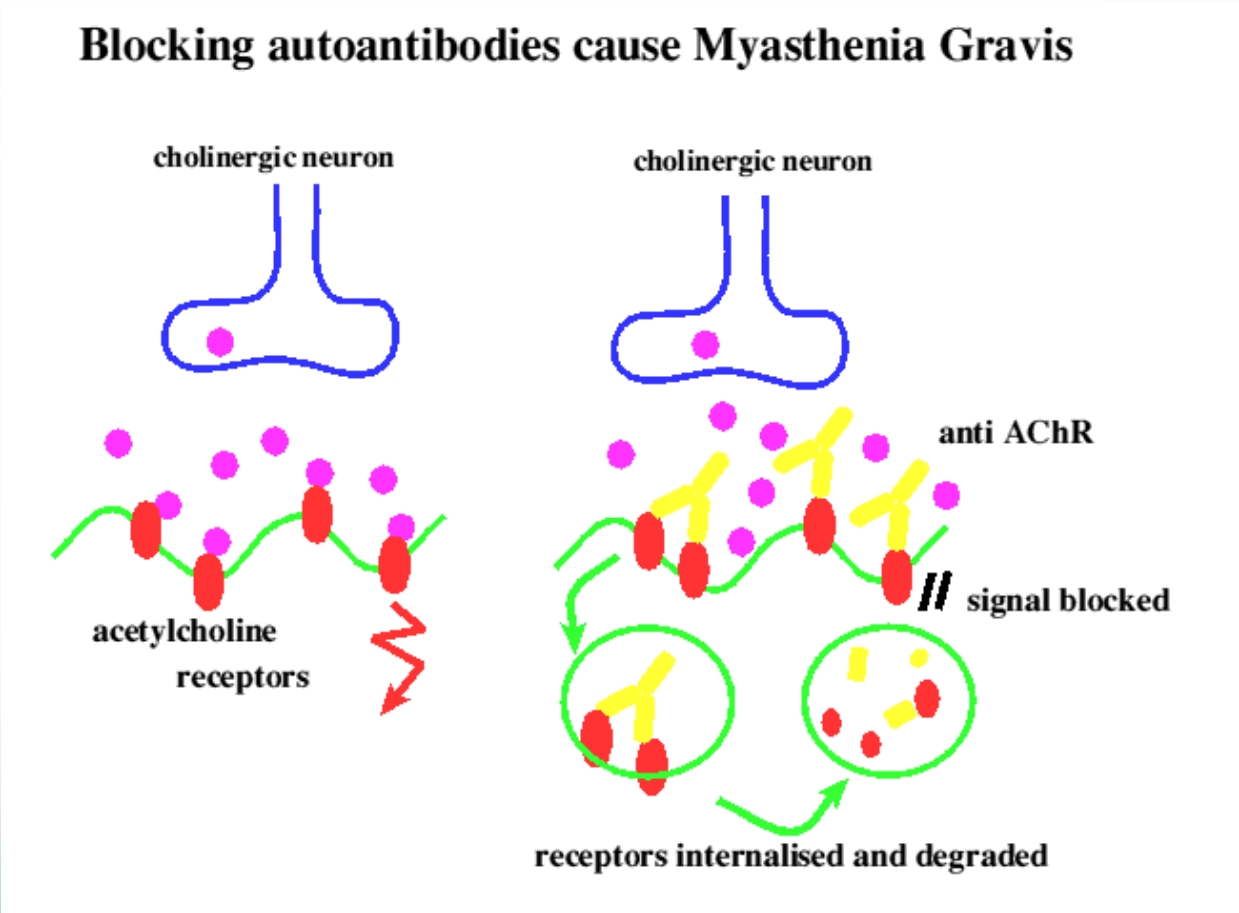
- Corticosteroids
- Other immunosuppressive treatment such as methotrexate or cyclosporine

Disorders of Neuromuscular Junction

Myasthenia Gravis

- Commonest disease of neuromuscular junction
- Caused by antibodies directed against postsynaptic acetylcholine receptors

Myasthenia Gravis



Clinical Features

- Onset after 1 year
- Adolescent girls most commonly affected
- Generalized form affects extraocular muscles first
- Then goes on to affect proximal limbs and bulbar muscles
- Variable natural course

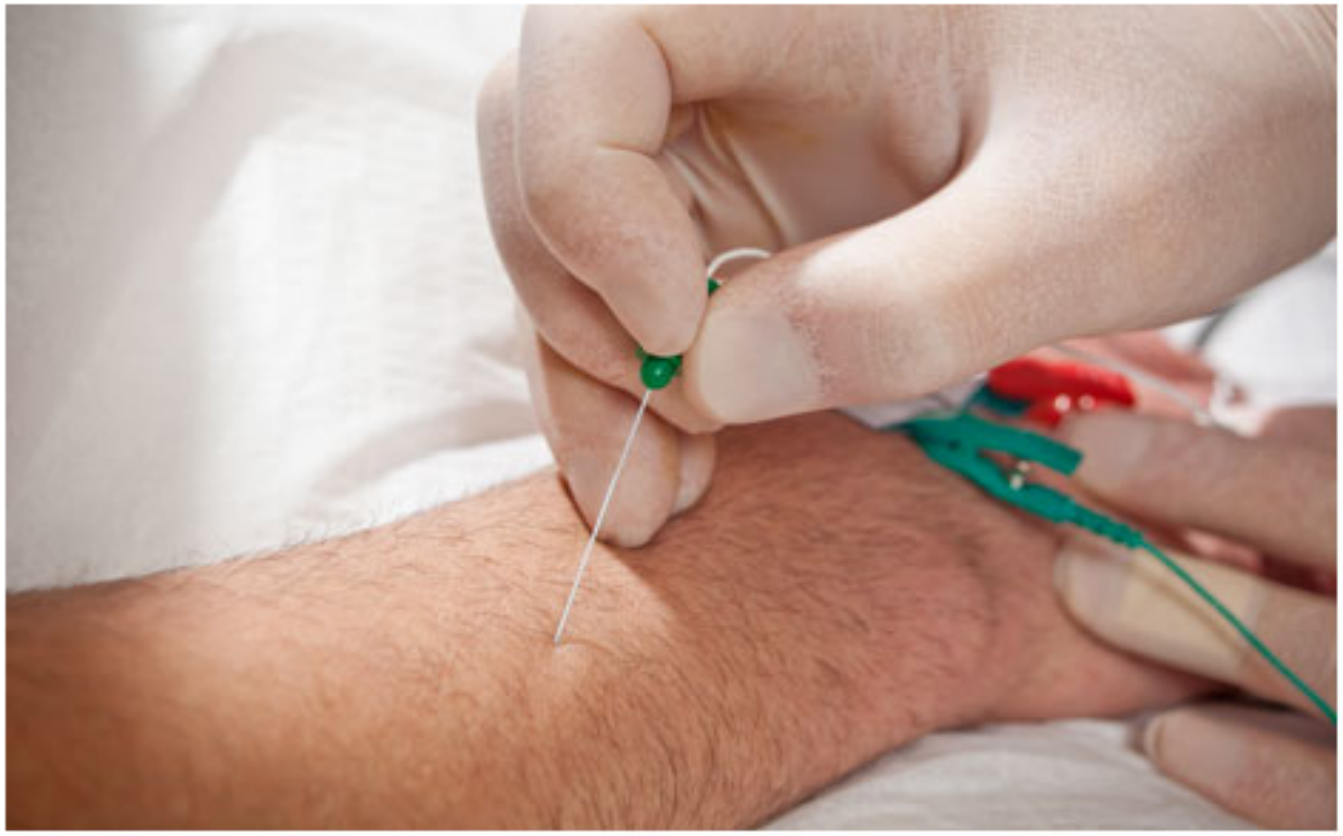
Diagnosis

- Edrophonium test
- Electromyography confirming neuromuscular block
- Demonstration of anti-acetylcholine receptor antibodies

Edrophonium test



Electromyography



Treatment

- Anticholinesterase drugs
- Immunosuppressants
- Thymectomy
- Plasma exchange or immunoglobulin infusion acutely

Meningitis

- Acute bacterial meningitis remains an important cause of neurological morbidity in child- hood. Causative organisms vary depending on the age of the child. The pattern of infection has been altered by changing immunization patterns.
- Age related organisms

Clinical features

- In neonates meningitis is usually part of a septicaemic illness. Symptoms and signs may be non-specific, e.g. lethargy, poor feeding, respiratory distress. Neck stiffness is rarely seen
- In young infants also, signs may be non-specific and meningeal irritation may be absent
- In older children, signs are more typical, lethargy, headache, photophobia, neck stiffness.
- Meningococcaemia is associated with a haemorrhagic rash

Outcome

- Neurological sequelae may occur in up to 30% of children - focal neurological deficits, learning disability, hydrocephalus and deafness may all occur
- Mortality is improving with earlier diagnosis and treatment

Diagnosis

- Lumbar puncture and CSF analysis are definitive
- White cell count is raised with a predominance of neutrophils, CSF glucose is reduced and protein is raised
- Gram staining of CSF and immunoassays may allow identification of the organism
- Lumbar puncture is contraindicated if there are signs of raised intracranial pressure or if consciousness is impaired. Treatment then needs to be aimed at the most likely organisms. Blood cultures can be taken before starting treatment

Management

- Antibiotic treatment - agent will depend on age of patient and probable infecting organism
- Watch for subdural effusions and hydrocephalus measure head circumference
- Evidence concerning steroid use to prevent neurological sequelae is unclear, some evidence to support the prevention of deafness in *Haemophilus influenzae* meningitis

Viral Meningitis

- Symptoms similar to bacterial meningitis, but less pronounced
- Specific diagnosis may be suggested by other disease stigmata
- CSF clear with lymphocytosis
- Prognosis of uncomplicated viral meningitis is good

Tuberculous Meningitis

- Generally occurs within 6-8 weeks of primary pulmonary infection or during miliary tuberculosis.
- Commonest in age range 6 months to 3 years.
- Leads to basal arteritis, which may cause hydrocephalus and cranial neuropathies.
- Symptoms otherwise are often non-specific, lethargy, fever, headache.
- CSF: high white cell count, predominantly lymphocytes, raised protein often > 2 dl, low glucose, tuberculous cultures may be positive.

Treatment

- Antituberculous chemotherapy
- Optimal treatment not determined
- Usually triple therapy (rifampicin, isoniazid, pyrazinamide) for at least 6 months but many authorities suggest a fourth drug for the first 2 months
- The place of corticosteroids in treatment is unclear but these are often used in the first
- few months to reduce inflammation
- Mortality and morbidity remain high despite treatment.

Encephalitis

- Herpes simplex encephalitis
- Common
- High mortality and high morbidity (50%)
- Acyclovir

Subacute Sclerosing Panencephalitis

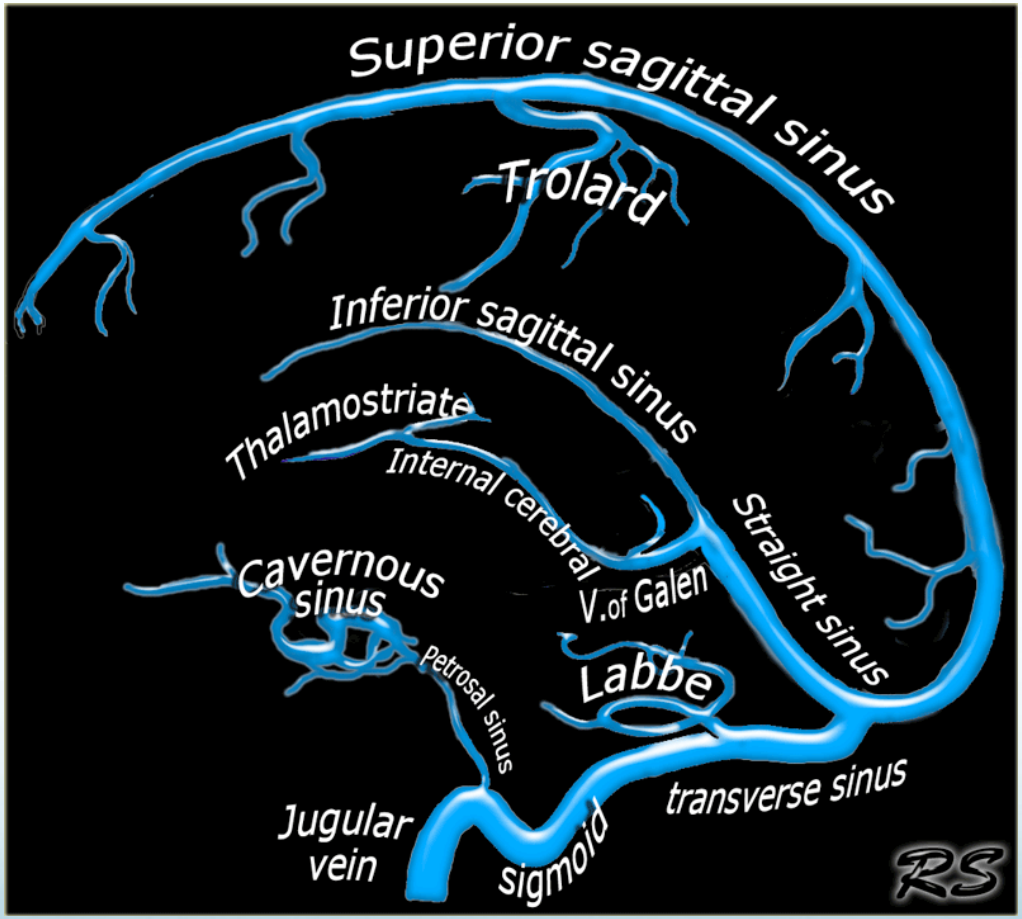
- A slow viral infection, caused by an atypical response to measles infection. Exposure to measles virus is usually in the first 2 years. Risk is higher after contracting natural measles, compared with that after measles immunization. Median interval between measles and subacute sclerosing panencephalitis is 8 years.
- Subtle deficits initially Increasing memory difficulties
- Worsening disabilities, seizures, motor difficulties, learning disability

Sydenham's Chorea

- Main neurological feature of rheumatic fever
- Chorea results from immune reaction triggered by Group A streptococcal infection
- May be associated with emotional lability
- Probably overlaps with PANDAS (psychiatric and neurological diseases associated with streptococcal infection)
- In about 75% of cases the chorea resolves within 6 months

Arterial occlusion

Venous thrombosis



Cerebral Vein Thrombosis



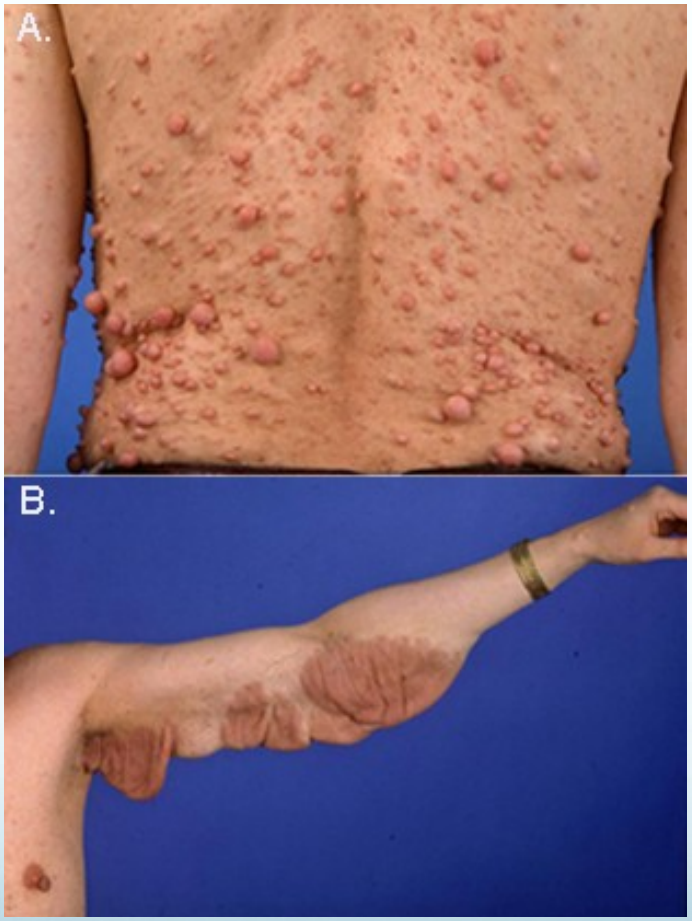
Neurofibromatosis

- Gene is localized to chromosome 17q11.2.
- **Diagnostic criteria** (two or more are necessary for diagnosis):
- Six or more cafe-au-lait spots > 5 mm in diameter in prepubertal patients and > 15 mm in postpubertal patients.
- Two or more neurofibromas or one plexiform neurofibroma

Neurofibromatosis Type1



Neurofibromas



Neurofibromatosis Type1

- Axillary or inguinal freckling
- Optic glioma
- Two or more iris hamartomas (Lisch nodules)
- Typical osseous lesions such as sphenoid dysplasia.
- First-degree relative affected

Flickering of the Skin



Iris Hamartoma



Optic Nerve Glioma



Neurofibromatosis Type 1

- **Neurological manifestations:**
- Macrocephaly
- Learning disability
- Epilepsy
- Optic gliomas

Neurofibromatosis Type 2

- Gene is localized to chromosome 22q11.2

- Diagnostic criteria:

- Bilateral VIIIth nerve neurofibromas
- Unilateral VIIIth nerve mass in association with any two of the following: meningioma, neurofibroma, schwannoma, juvenile posterior capsular cataracts
- Unilateral VIIIth nerve tumour or other spinal or brain tumour as above in first-degree relative

Neurofibromatosis Type 2



Tuberous Sclerosis

- Dominantly inherited disorder with variable expression. Characterized by skin and central nervous system abnormalities, although there may be cardiac, renal and bony abnormalities as well. At least two mutant genes on chromosomes 9p34 ***(TSC7)***and 16p13 ***(TSC2).***

Clinical Features

- Seizures
- Neurodevelopmental impairment
- Cutaneous manifestations
 - Adenoma sebaceum
 - Periungual fibromata
 - Hypopigmented patches
 - Shagreen patch

Adenoma sebaceum





Ash Leaf



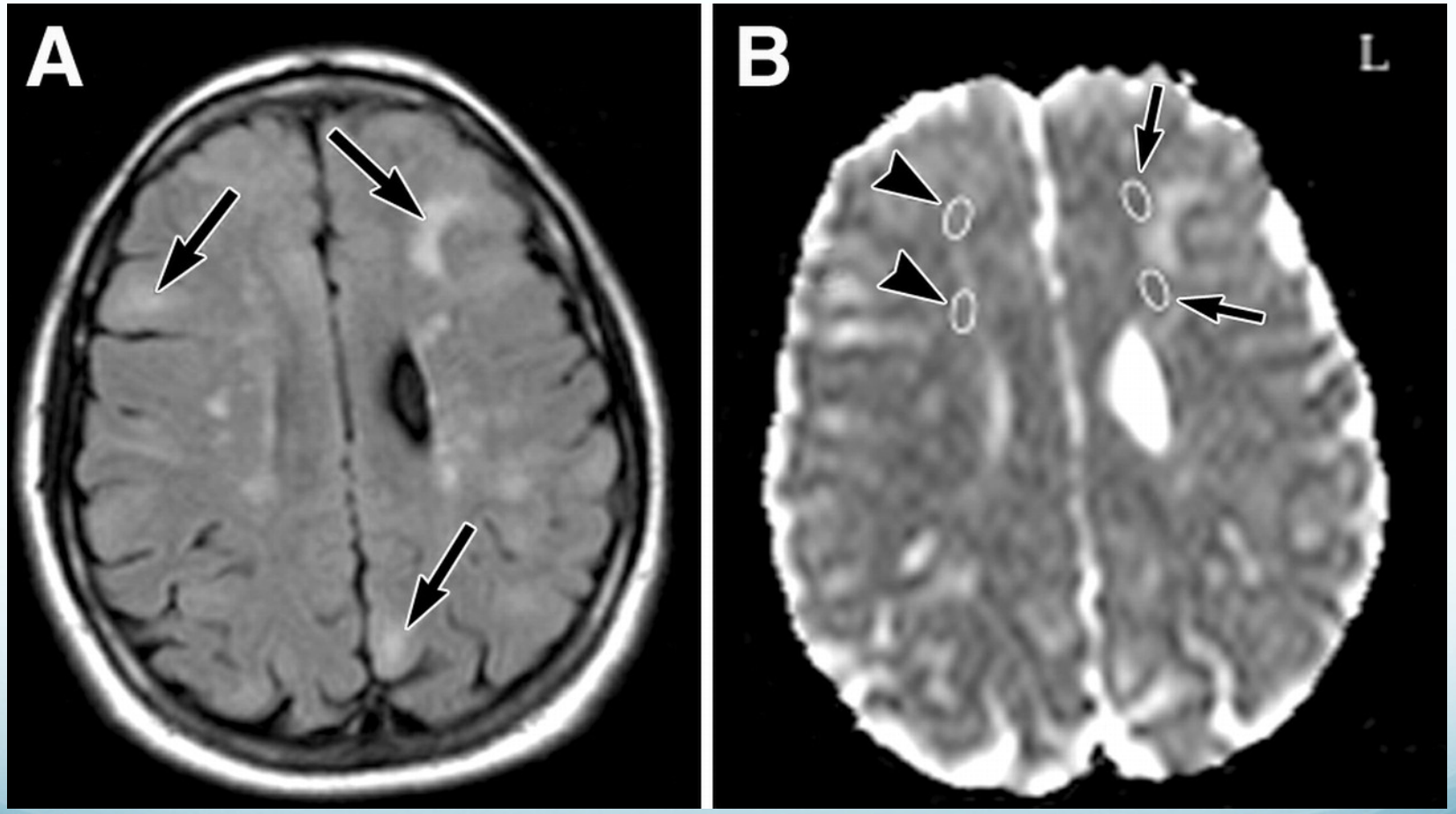
Shagreen Patch



Clinical Features

- Retinal hamartomas
- Renal angiolipomatas
- Cardiac rhabdomyomata

TS Brain



Ataxia Telangiectasia

- Characterized by conjunctival telangiectasia, progressive cerebellar degeneration and immunological impairment.
- Multisystem disease with autosomal recessive inheritance.
- Responsible gene, at least in some families, is mapped to chromosome 11q22-23.

Clinical Features

- Progressive ataxia
- Scleral telangiectasia
- Abnormalities of cell-mediated and humoral immunity leading to increased sinopulmonary infections
- High incidence of reticuloendothelial malignancies in later life

Diagnosis

- Elevated a-fetoprotein level
- Reduced IgA
- Reduced IgD
- Inversions and translocations involving chromosomes 7 and 14
- Gene mutation analysis

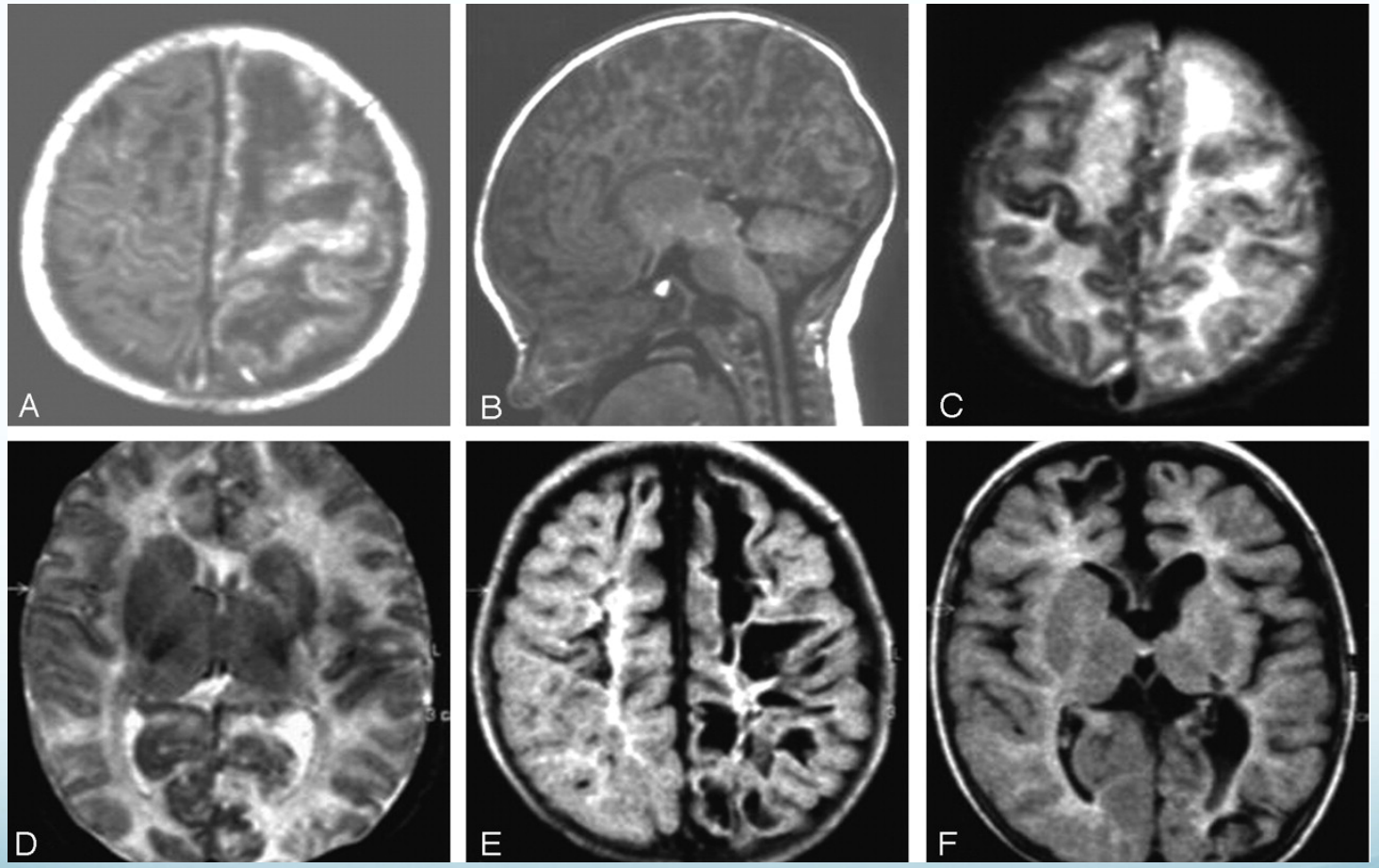
Incontinentia Pigmenti

- Rare
- Probably inherited as X-linked dominant
- Characterized by skin lesions initially erythematous, papular, vesicular or bullous lesions on trunk and limbs, then pustular lesions, then pigmented lesions
- 30-50% of neurological features: Seizures & encephalopathy
- Eye lesions in 30%
- -

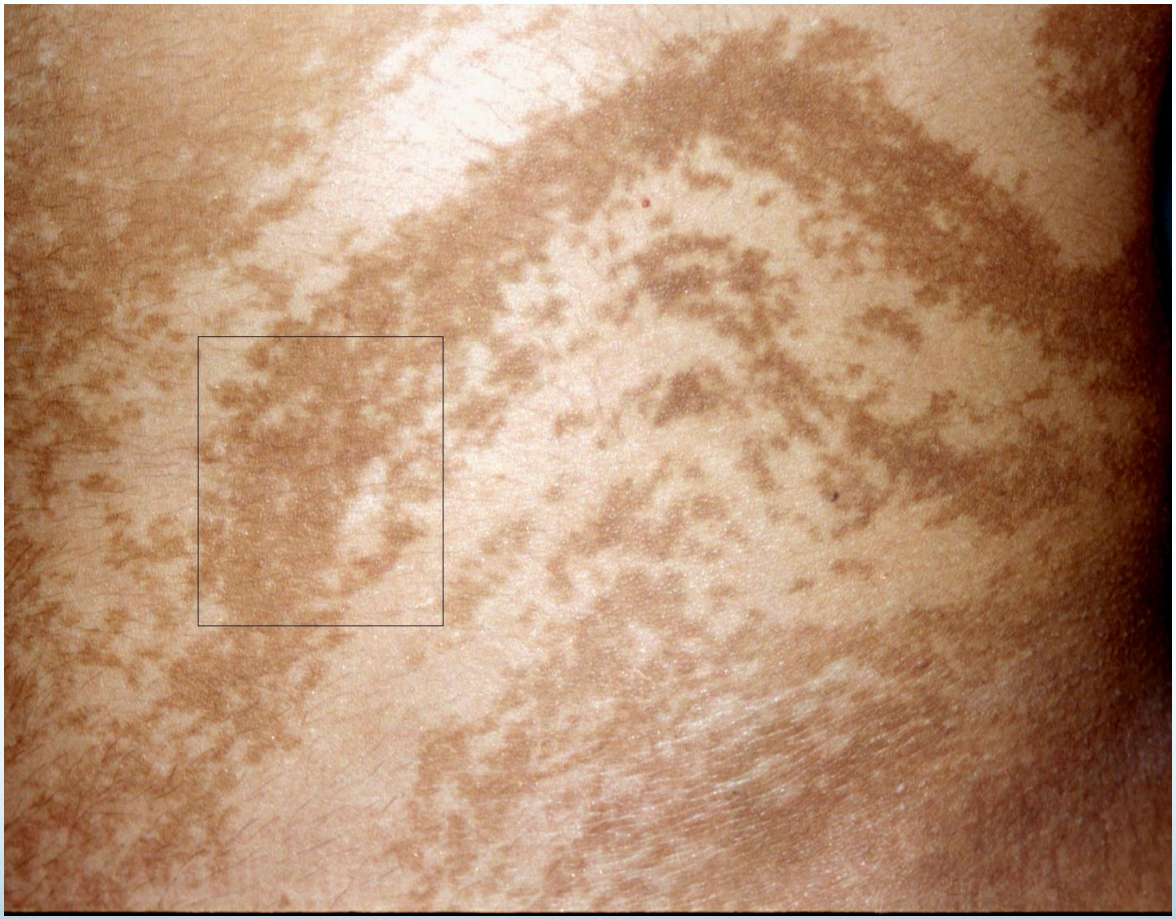
Incontinentia Pigmenti



Incontinentia Pigmenti



Hypomelanosis of Ito



Hypomelanosis of Ito

- Also rare
- Sporadic inheritance
- Hypopigmented areas
- Central nervous system involvement common including seizures and hemimegalencephaly

THANK YOU